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LECTURE NOTES ON PHYSIOLOGY

BY
HENRY H. JANEWAY, M.D.

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THE CIRCULATION

THE BLOOD

Its Functions in General—The blood performs two important functions—

1. The transportation of, first, substances needed for the nutrition of the body and for the supply of energy to the various tissues, and, second, of substances representing waste products no longer of use to the tissues.

2. The supply of a uniform chemical and thermal environment around all the cells of the body.

Manner of Circulation of the Blood—The blood in performing these functions circulates in a system of closed tubes. It never comes into direct contact with the tissues. All interchanges between the blood and the cells of the body are accomplished through vascular walls of extreme thinness—a single layer of endothelial cells—which form the walls of smallest blood vessels, the capillaries.

Uniform Composition of the Blood—In virtue of its functions of conveying chemical substances for the supply of energy and for the repair of tissue waste the composition of the blood arriving at an organ must differ, and does differ, from that leaving an organ. The degree, however, of variation in the composition of the blood is so slight that it is almost negligible. The preservation of its uniform character is guarded by a most sensitive mechanism in order that the second function served by the blood may be accomplished, namely, that the cells of the body may be surrounded by a uniform environment.

The Red Blood Cells—1. Red blood corpuscles are biconvex circular discs 7.1 to 7.8 microns in diameter by 2.5 microns in thickness at the periphery and 1.0 to 2.0 microns at their centers. Each corpuscle is pale yellow in color, but when crowded together in a suspension such as occurs in fluid blood they impart a red color to the fluid. In mammals the blood cells have no nucleus and

are circular. There are normally 5,000,000 red blood cells to each cu. mm. of fluid blood. (Fig. 1.)

The White Blood Cells—White blood cells are colorless, granular, nucleated cells resembling in every way the unicellular ameba.

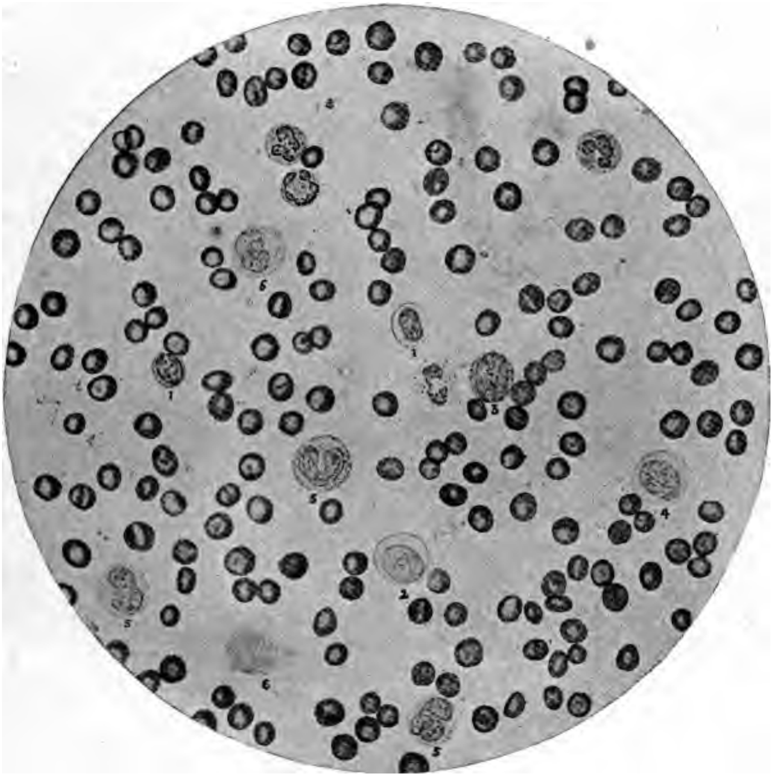


Fig. 1.—Field Showing Red Blood Cells and a Variety of White Cells.

1, Small lymphocyte; 2, Large lymphocyte; 3, Large mononuclear cell, quite different from a transitional cell; 4, Large mononuclear cell, closely resembling a transitional cell; 5, Transitional cell; 6, Degenerated cell. Although 4 definitely and 3 quite probably belong to the transitional cell group, both were included with 2 and classed with the mononuclear cells. Three typical polynuclear cells are shown in the upper part of the field.

They possess the ameba's power of locomotion by throwing out pseudopodia and of ingesting and digesting certain foreign bodies and bacteria.

Most of the colorless cells are a little larger than the red cells.

They are present normally in the blood in the ratio of from 1 to 1000 to 1 to 500 of the number of red cells.

The Blood Plaques—A third corpuscular element in the blood is the blood plaque. These are small circular disc-like bodies of about one-third the size of the red blood cell. The bodies stain a deep blue with the basic anilin dyes and appear to be connected very closely with the process of clotting of the blood. They appear to increase in number in shed blood and to serve as centers for the formation of a network composed of web-like strings called fibrin. In the fluid blood all these elements are suspended in a fluid called plasma.

THE RED BLOOD CELLS

The Red Blood Cells in Greater Detail—*A. The Surface Area of the Red Blood Cells*—The total area of all the red cells in a man of average weight is approximately 3,000 square meters, or 1,500 times the total surface of the body itself. The combined red cells, therefore, offer abundant surface for the absorption of oxygen.

B. Osmotic Relations of the Red Cells—Unless the blood cells are suspended in a solution of salts isotonic with the blood plasma they will not preserve their form. The membrane of the red cell is semipervious to sodium chlorid. If red cells are suspended in a solution of sodium chlorid which is stronger than one which is isotonic with the blood plasma (.9 per cent.), water will pass out of the red cell, causing the latter to shrink. If the solution of sodium chlorid is weaker than this strength, water will pass from the solution into the red cell, causing it to swell, and if sufficiently weak or if the cells are placed in water the red cells will swell up till they burst and thus liberate their hemoglobin or red coloring matter, which passes into solution in the water or weak salt solution. Most neutral salts like sodium chlorid do not pass through the membrane of the red cells.

To urea the cell membrane is pervious. It behaves toward urea as toward water. The cell membrane is also pervious to alcohol, ether and chloroform.

C. The Cell Membrane—The cell membrane is composed of a cholesterin and lecithin compound.

Laking of Blood—Substances Which Rupture the Membrane

of the Red Cell and Which Lake Blood—The rupture of the cell membranes of the red blood cells and the obtaining of the hemoglobin or coloring matter of the red cells in solution is termed laking. Though the hemoglobin easily passes into solution, its combination in the red cell is probably solid.

The following substances will lake blood—

1. Ether.
2. Water.
3. Alternately freezing and thawing of blood.
4. Bile salts.
5. Certain foreign serums and other bodies termed hemolysins.

D. The Stroma of the Red Cells—The stroma may be separated by centrifuging and laking the centrifuged deposits and again centrifuging and washing the sediment of corpuscles with acid sodium sulphate.

The stroma protein of the red cells forms only 4 per cent. of the total solids of the red cell. This protein may be broken up by gastric digestion into a protein portion and a body rich in phosphorus. The latter is a nuclein. The nuclein yields the purine bases. The original protein is, therefore, a nucleo protein. The stroma also contains lecithin and cholesterin.

Hemoglobin and Its Compounds—Hemoglobin may be obtained by laking blood as previously described. Its characteristic chemical reaction, which is of physiological importance, is its property of forming an unstable combination with oxygen and to some extent with carbon dioxid.

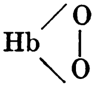
Oxyhemoglobin—The combination with oxygen is called oxyhemoglobin, and hemoglobin minus the oxygen is called reduced hemoglobin. Simple cooling of solutions of hemoglobin to 10° C. may suffice for crystallization of the hemoglobin. The process may be facilitated by the addition of alcohol to 25 per cent. The best method is to precipitate the globulins by adding a sat. sol. of ammonium sulphate, filtering and then cooling.

Iron forms about .333 to .336 per cent. of the hemoglobin and is very constant in its amount among various animals. From this percentage it is possible to calculate the approximate size of the hemoglobin molecule. Its atomic weight calculated by this method *is 16,660.*

The oxygen may easily be separated from a solution of hemoglobin by exposing the same in a Torricellian vacuum. The combination with the oxygen is, therefore, a very loose one.

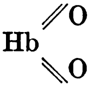
Methemoglobin—The oxygen, however, may be combined with the hemoglobin in a much more stable matter. This combination is called methemoglobin. It is formed in the human body whenever hemoglobin is suddenly liberated. It may be prepared by adding to a solution of oxyhemoglobin an oxidizing or reducing agent such as a ferricyanide or nitrate or permanganate. In any case its formation means two chemical changes. The first of these changes is the liberation of the hemoglobin and the second change is a stable union of the reduced hemoglobin with the oxygen from the oxidizing agent or the free oxygen in the absence of other special oxidizing agents. The following formulas will illustrate two different ways in which oxygen may be combined with hemoglobin:

Oxyhemoglobin



or

Methemoglobin



It is alleged that methemoglobin contains only one-half as much oxygen as oxyhemoglobin. In the second formula the union would form a more stable combination, such as, for instance, is represented by methemoglobin.

Carbon Monoxid Hemoglobin.—If hemoglobin is placed in an atmosphere of carbon monoxid the radical carbon monoxid unites with the hemoglobin, forming carbon monoxid hemoglobin. This is a compound of far greater stability than oxyhemoglobin, so that when exposed to oxygen the latter will not replace the carbon monoxid. The color, however, of carbon monoxid hemoglobin is a bright red, like oxyhemoglobin; hence it is that people poisoned with carbon monoxid may appear of a good color and yet be suffering from deficient oxygenation of the blood. Moreover, supplying them with oxygen in liberal quantities does not result in the formation of oxyhemoglobin and consequently does not relieve the *anoxemia.*

These four compounds, oxyhemoglobin, reduced hemoglobin, methemoglobin and carbon monoxid hemoglobin, are definite chemical substances of great physiological importance and each have their own characteristic spectra. (Fig. 2.)

Oxyhemoglobin gives two absorption bands between the lines C and D. Reduced hemoglobin gives one broad absorption band between the two lines C and D, and carbon monoxid hemoglobin gives again two lines very similar to oxyhemoglobin, but the center of each band is nearer to the red end of the spectrum.

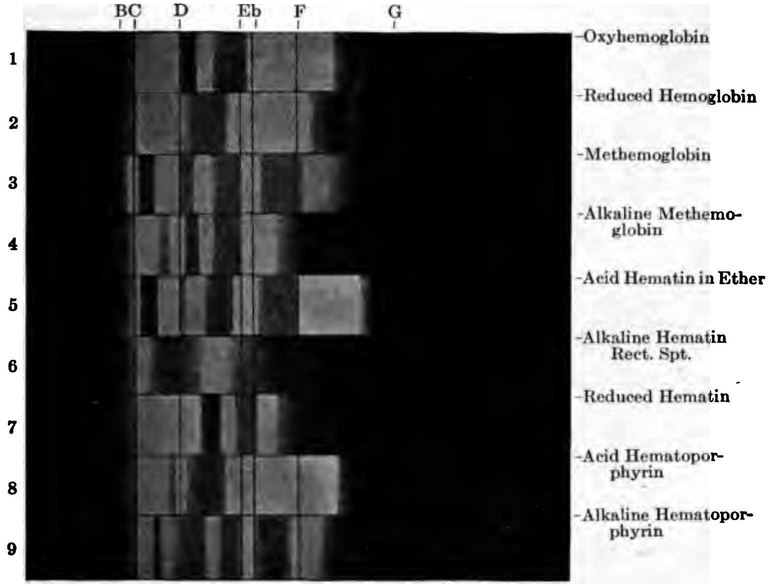


Fig. 2.—Spectrum of Hemoglobin and Its Derivatives (Mac Munn).

The Chemical Nature of Hemoglobin—Information upon the chemical nature of hemoglobin can only be derived by a study of its derivatives.

Treated with weak acids or alkali or heated to 70° C., hemoglobin may easily be split into a protein portion and an iron containing colored portion, the prosthetic group. The protein portion is classified with the histones. About 94 per cent. of hemoglobin is this protein, and the chromogenic group forms about 4.5 per cent. and is called hematin.

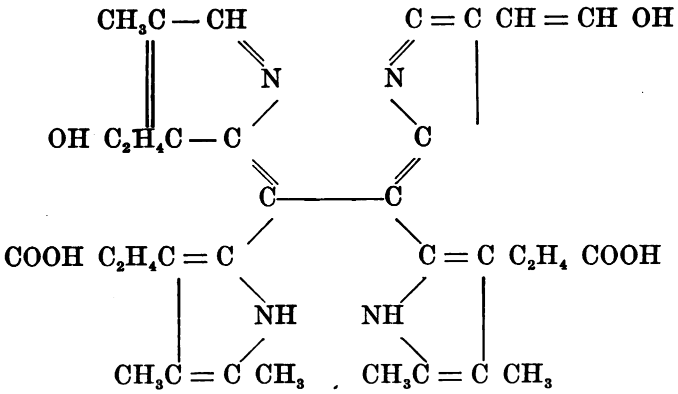
A. Hematin.—Hematin may be more readily obtained from the hydrochlorid of hematin, which is known as hemin. The latter can be obtained by heating blood, even a very small quantity, as a dried blood stain, with acetic acid and sodium chlorid. It separates as well-defined reddish brown needle-like crystals, which are so characteristic that obtaining them has been used as a test for blood stains.

Hematin forms compounds with acids and alkalis which are known as acid and alkali hematin. Both of these give characteristic absorption bands in the spectrum.

B. Hemochromogen.—Ordinary alkali hematin may be reduced by reducing agents such as ammonium sulphid to form another body known as reduced alkali hematin. The last may be separated directly from blood by the preparation of hematin by means of an alkali in the presence of reducing agents. This reduced alkali hematin is called hemochromogen. It also gives a characteristic spectrum, even in dilutions of 1-25,000th parts of water, and is of much importance, as it represents the portion of hemoglobin capable of forming loose combinations with oxygen. This view is further confirmed by the possibility of obtaining carbon monoxid hemochromogen by treating carbon monoxid hemoglobin with alkalis in the presence of a reducing agent.

C. Hematoporphyrin—Hemin contains one atom of chlorin and one atom of iron. Hematin contains one atom of iron. When hematin is treated with concentrated sulphuric acid the atom of iron is split off and the resulting body is called hematoporphyrin. This body possesses a formula which is isometric with bilirubin, the chief pigment contained in bile, and also gives a characteristic spectrum.

D. Hemopyrrol—From hematoporphyrin can be obtained three substances known as hemopyrrols, the mixture of which gives reactions which are also given by urobilin. These same substances may be also obtained from the chlorophyll of plants. The formula of each of these three substances is known, and, according to Willstätter, hematoporphyrin is formed of four pyrrol groups united together. A knowledge, therefore, of the derivative of hemoglobin makes possible an understanding of its chemical structure. Willstätter gives the following structure formula for hematoporphyrin:



The relationship between hemoglobin or its derivatives and the chief pigment of the bile and urine is significant as regards the origin of these latter substances from the blood pigment. The relationship between hemoglobin, the oxygen-carrier of the animal body, and chlorophyll, the deoxidizer of the carbon for plant life, is also of interest.

The Probable Chemical Structure of Hematin—To obtain hemin from hematoporphyrin the insertion of one atom of iron and chlorin is all that is necessary.

Hematin is to be regarded as identical with oxyhemochromogen and is a far more stable body than reduced alkali hematin or hemochromogen, in so far at least as the iron concerned. In the case of oxyhemochromogen or ordinary hematin only the strongest acids can split off the iron, which is not the case with reduced alkali hematin.

Reduced hematin seems to be a simple combination of iron and hematoporphyrin and can be easily prepared synthetically from these two components. It is possible to affect a combination of globin and hemochromogen and also a combination of other proteins with hemochromogen. Other proteins may then replace the globin in combination with the chromogenetic group of the red cells.

Source of the Red Cells—In the embryo the first red blood cells are formed by the differentiation of the mesenchymic cells from which the first blood vessels are formed. A similar growth of red cells of the fetus occurs in liver and spleen and later in the bone marrow. During the earlier periods the majority of red cells

are nucleated. As full term is reached the nucleated cells become less and less frequent, until at birth practically all of the cells are of the non-nucleated type.

Provision must exist in the adult for the continued formation of red cells, if merely to replace those which are lost or destroyed by hemorrhage, other accident or disease. A sensitive mechanism in the healthy adult or growing child keeps the number of red blood cells constant. In health pigment which is derived from the red cells is constantly leaving the body in the urine and feces. This steady loss must be repaired. The site of repair is the bone marrow.

The structure of bone marrow eminently fits it for this function. It forms a rigid tissue protected from pressure and composed of large spaces through which a slow circulation may occur. In this tissue one may find all stages from the marrow cells to the fully formed red blood cell. The marrow of the bones is the only tissue which is seen to undergo alteration when blood cell formation is stimulated by hemorrhage. Within it all stages between certain nucleated marrow cells and the non-nucleated red cells are found. Many nucleated red cells are found within the marrow, and after hemorrhage these gain access to the general circulation.

The portions of the marrow which are red are those chiefly engaged in the formation of the red cells. Under normal conditions the red marrow occupies only the epiphyses of bones, but when a demand for increased formation of red cells exists the red portion of the marrow extends longer or shorter distances into the shaft.

The length of life of the red blood cell is unknown; sooner or later each red cell must perish. As it becomes older disintegration sets in and the corpuscle becomes a prey to the process of phagocytosis. In the hemolymph glands and in the spleen, fragments of red cells may be recognized within the bodies of phagocytic cells.

The liver obtains its supply of pigment for the manufacture of bile from the disintegrated red cells. The liver also contains much iron. Both an increased secretion of bile and storage of iron within the liver may be caused by injecting hemoglobin or by those conditions leading to rapid destruction of the red blood cells. In some cases actual hemoglobin crystals have been observed within the liver. We must, therefore, regard the liver as the chief place of destruction of the red blood cells.

THE WHITE BLOOD CELLS

Varieties of the White Cells—These are colorless, granular or hyaline cells capable of ameboid movement, varying in size, but the majority are larger than the red blood cells. Normally there are 5,000 to 8,000 in every cu. mm. of blood. They are classified into the following varieties. (Fig. 3.)

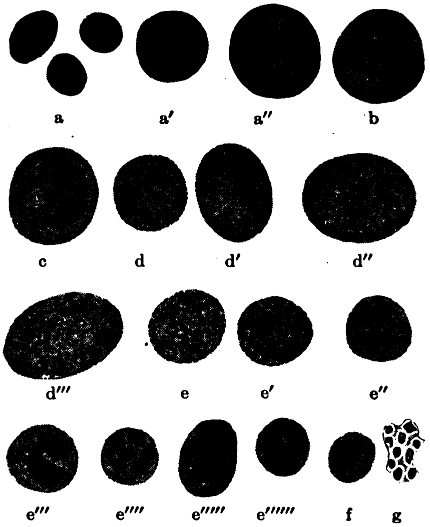


FIG. 3.—a, Lymphocytes; a′, a″, large lymphocytes; b, large mononuclear lymphocyte; c, transitional leukocyte; d, eosinophil myelocyte (bright red granules); d′, d″, neutrophil myelocyte (brown granules); d‴, basophil myelocyte (blue granules); e, e′, polynuclear eosinophil; e″, e‴, e⁗, polynuclear neutrophil leukocyte; e⁗′, e⁗″, polynuclear basophil leukocyte; f, small neutrophil pseudolymphocyte; g, blood-platelets.

Polymorphonuclear Cells.—Multinucleated or lobed nucleated cells. Relatively to the size of the nucleus there is considerable protoplasm in which are numbers of neutrophile granules, that is, they do not stain a bright red with eosin or a blue with methylene blue, but rather a brown color, indicating a position between the granules, reacting to basic and acid dyes. These cells form 70 per cent. of the white blood cells in the normal individual.

Cells with an Hourglass or Horseshoe-shaped Nucleus and Only

a Few Neutrophile Granules—These may be regarded as transitional cells between the hyaline white cell and the polymorphonuclear white blood cell. They form about 1 per cent.

Lymphocytes—Small cells with a deeply staining nucleus, around which is only a small amount of hyaline protoplasm. They form 23 per cent. of the white blood cells.

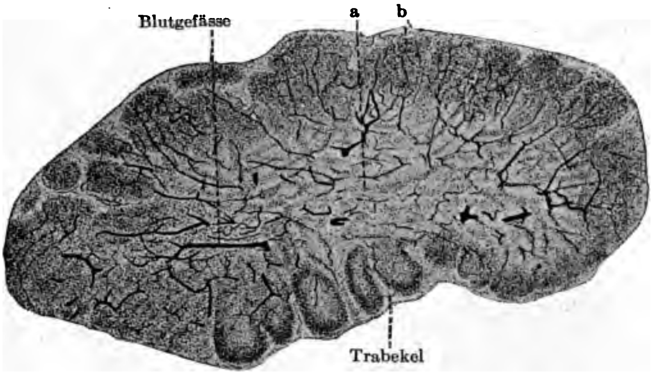


FIG. 4.—SECTION THROUGH A MESENTERIC LYMPH GLAND OF A CAT OF WHICH THE BLOOD VESSELS HAVE BEEN INJECTED. MAGNIFIED 50 DIAMETERS. It shows well the central sinuses (a) and the cortical follicles (b).

Large Mononuclear or Hyaline Corpuscles, Very Large Cells, Two and Three Times the Diameter of a Red Cell—They possess a large feebly staining nucleus, around which is a relatively large amount of hyaline very faintly staining protoplasm; 2 per cent. are normally present.

Eosinophile Cells—A large cell with a lobed crescentic or reniform nucleus and a surrounding protoplasm in which are imbedded many large size granules, taking a deep or eosin stain, and hence appearing a bright red. They are normally present to the extent of .5–2 per cent.

Mast Cells—These cells have a lobed nucleus, but large basophilic granules, taking a deep stain with methylene blue. They form about one-half of one per cent. of the total number of white blood cells.

The Site of Origin of the White Cells—Origin of the white blood cells is not the same for all varieties of white cells. The *lymphocytes come from* the lymph glands. Each gland consists of

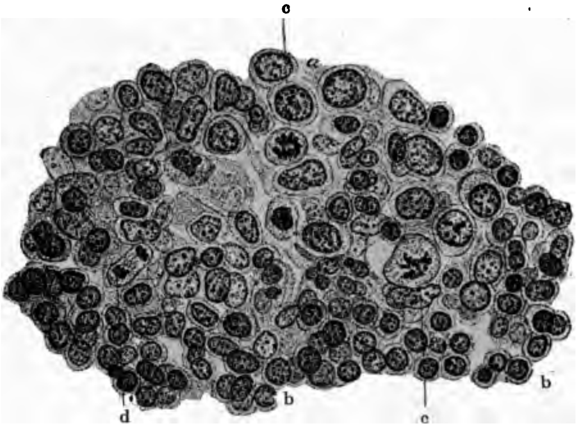


FIG. 5.—A SECTION THROUGH A GENERATIVE CENTER OF A CORTICAL NODULE OF A LYMPH GLAND, SHOWING CELLS IN MITOTIC DIVISION.

a, Large mononuclear leukocytes; b, small lymphocytes which are especially numerous near the lower borders of section; c, monaster of the metaphase of a dividing cell; d, diaster or anaphase of a dividing cell. (Kolliker.)

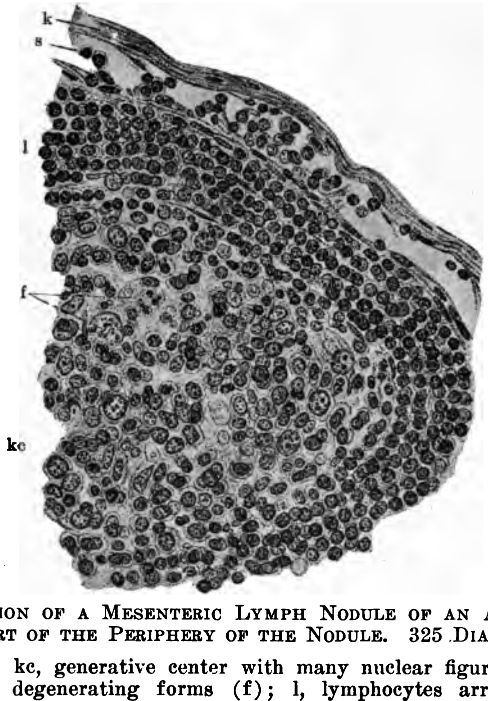


FIG. 6.—SECTION OF A MESENTERIC LYMPH NODULE OF AN ADULT, SHOWING A PART OF THE PERIPHERY OF THE NODULE. 325 DIAMETERS.

k, capsule; kc, generative center with many nuclear figures, a number of *cells showing* degenerating forms (f); l, lymphocytes arranged in rows; *s, lymph sinus. (Kolliker.)*

a central portion, consisting largely of lymphatic vessels between trabeculæ and filled with lymph, and in which are suspended lymphoid cells. The periphery of the gland is composed of nodules of lymphatic tissue. (Figs. 4, 5.) In the center of these nodules the lymphocytes are produced; these centers are known as the germ areas, and in them the cells are larger, stain less intensely and show frequent mitotic figures. The periphery of the nodule consists of a series of anastomotic channels communicating with one another and with the channels in the center of the whole lymphatic gland, which leads to the hilum or the end of the gland, from which the efferent veins leave the gland and convey the new cells produced by the gland to the blood stream. The arterial supply of the gland also enters at the hilum. (Fig. 6.)

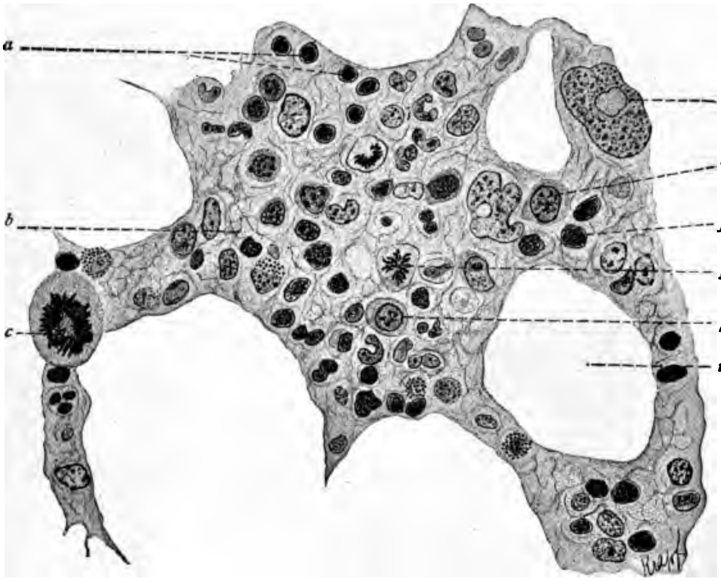


FIG 7.—FROM A SECTION THROUGH HUMAN RED BONE-MARROW. X680.

a, f, Normoblasts; b, reticulum; c, mitosis in giant cell; d, giant cell; e, h, myelocytes; g, mitosis; i, space containing fat cells. (Bohm, Davidoff, Huber.)

The polymorphonuclear leucocyte and eosinophile cells are derived, like the red blood cells, from the bone marrow. It is doubtful whether the hyaline white blood cell is derived by a trans-

sent in frogs' and birds' blood and from defibrinated mammals' blood, and their existence in the freely circulating blood has been questioned, because it is possible to obtain uncoagulated blood, for instance, within a platinum loop kept at body temperature, in which they are also absent. In the uncoagulated blood obtained in this *manner no blood platelets* exist on microscopical examination, and

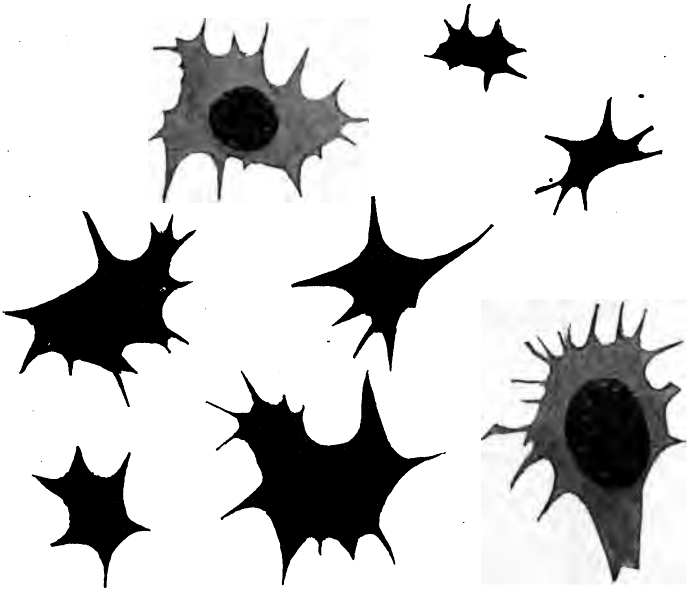


FIG. 8.—BLOOD PLATELETS FROM HUMAN BLOOD, STUDIED IN DEETJEN'S SOLUTION AFTER FIXATION WITH 1% OSMIC ACID AND STAINED WITH HEMATOXYLIN. 3,200 DIAMETERS. (Rauber-Kopsch.)

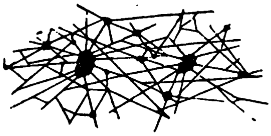


FIG. 9.—NETWORK OF FIBRIN, SHOWN AFTER WASHING AWAY THE CORPUSCLES FROM A PREPARATION OF BLOOD THAT HAS BEEN ALLOWED TO CLOT.

Many of the filaments radiate from small clumps of blood-platelets. (Schäfer.)

yet when such specimens cool the platelets make their appearance.

The platelets may be separated by first centrifuging off the red and white cells from the plasma which has been rendered non-coagulable by the addition of sodium oxalate or peptone. If plasma is cooled to 0° C. a precipitate indistinguishable from the platelets forms. Probably, therefore, the platelets do not exist as such within the circulating blood. Those fluids which display them best probably do so because they form them and not because they preserve them. The platelets are virtually a precipitate. After formation they rapidly undergo disintegration.

COAGULATION OF BLOOD

Conditions Preventing Coagulation—1. Within an excised ligatured vein the blood will remain fluid sometimes for days.

2. Birds' blood does not clot unless it comes into contact with the tissues. It may be obtained with care in a glass beaker without having come into contact with the tissues, and will remain fluid.

3. If blood is received into vessels coated with oil or paraffin and, if scrupulous care has been exercised to exclude dust, clotting may be prevented for hours.

4. Blood cooled to 0–1° C. and kept at this temperature will remain fluid indefinitely.

5. Sodium oxalate or sodium citrate added in strength of 1–1.5 per cent. will prevent clotting.

6. 0.3 gram of peptone per kilo of body weight injected into an animal will prevent clotting. The blood must be drawn off immediately, as the peptone causes a rapid death of the animal.

7. The addition of leech extract or hirudin will prevent clotting. It may be injected into the blood stream or mixed immediately with blood as it is drawn.

8. Cooled horses' plasma which has been allowed to stand will not clot upon raising the temperature if the plasma is filtered through two layers of filter paper.

After warming the addition to the filtrate of the washing of a blood clot or tissue extracts or a little fresh serum will cause clotting in such cooled plasma.

***First* Conclusion on the Mechanism of Clotting—Lime Salts**

Essential—Oxalate plasma will clot on the addition of calcium chlorid. The addition of the lime salt causes a precipitate of calcium oxalate; the blood will not coagulate until the calcium chlorid has precipitated all the oxalate and exists in a slight excess in the blood.

The first conclusion on the process of clotting is, therefore, that lime salts are necessary for the process. It is further necessary that the lime salts should exist in the form of a salt, in an ionized condition, as, for instance, calcium chlorid or calcium sulphate. Its mere presence in solution as in the form of a double soluble salt, which, for instance, is formed between the normal lime salts of the blood and sodium citrate, when the latter is used to prevent clotting, is not sufficient to permit clotting.

This explains why sodium citrate, which does not precipitate the calcium of the blood, will still prevent clotting.

Second Conclusion—Fibrinogen Necessary—The second conclusion on the process of clotting is that a globulin, fibrinogen, which is present in plasma but not in serum, is necessary for the process. Fibrinogen may be separated from oxalate plasma by half saturation with common salt. It separates as a granular precipitate at first and then as a stringy, slimy mass, which may be taken out by stirring on a glass rod, washed with the salt solution and redissolved in distilled water. It may be precipitated by warming to between 56–60° C. from either its pure solution or from the original plasma. No precipitate may be obtained from the serum left over until it is heated to 68° or 70° C. If a few drops of calcium salts are added to the solution of the separated and only partially washed fibrinogen, redissolved in water, it rapidly clots.

Third Conclusion—Another Body, Thrombin, Necessary—Something else besides the calcium and fibrinogen is necessary for clotting. A solution of thoroughly washed fibrinogen will not clot upon merely the addition of lime salts; but can be made to clot upon the addition of either a little serum or the washings from a blood clot or the watery extract of an alcohol coagulated serum. The substance which is added in the serum or washings is called thrombin. It has been called fibrin ferment, but the fact that accurate experiments show that it is used up in the process of clotting, even though it acts in extremely small quantities, and *the fact that its action* on fibrinogen is almost independent of

temperature have been accepted by some observers as evidence though hardly sufficient evidence that it is not a ferment.

Fourth Conclusion—Thrombin Is Formed from a Prothrombin—The part played by calcium in the process of clotting is in connection with the formation of thrombin. This is true because thrombin and fibrinogen will form a clot when mixed together in the entire absence of calcium salts, but the substance which with the calcium forms thrombin and which we may call prothrombin may be separated from oxalate plasma by allowing it to stand at 0° for two or three days and then filtering through several layers of filter paper. It is possible to prepare pure thrombin by extracting fibrin with 8 per cent. solutions of sodium chlorid and getting rid of the proteins by shaking with chloroform. The filtrate left by filtering the cold oxalate plasma will not coagulate upon the addition of lime salts, but if we treat the precipitate with a little calcium chlorid and add it to the filtrate a clot will form. More than this, a clot will be obtained if the precipitate, provided it is not thoroughly washed, plus a little calcium is added to a pure solution of fibrinogen.

Fifth Conclusion—Thrombokinase and Thrombogen Are Necessary—Two substances beside the calcium salts are necessary for the formation of thrombin; only one of these may properly be designated as prothrombin. It will be a little better to designate it now as thrombogen. It has been said that a precipitate formed in the cold will produce a clot with fibrinogen in the presence of calcium. This is only true if the precipitate is not thoroughly washed, though, even if thoroughly washed, it will produce a clot in the plasma filtrate. Two substances, therefore, are necessary, not merely the precipitate but another substance contained in the plasma, of which sufficient adheres to the precipitate produced by cold to form with it, in the presence of calcium, thrombin. Extracts made from tissues can be shown to contain the same substance which exists in the washed precipitate formed from oxalate plasma by cold. These extracts in the same manner as the precipitate will form a clot when mixed with oxalate plasma, together with lime salts, but will not form a clot in solutions of fibrinogen unless a little plasma is also added to the solution of fibrinogen.

The substance contained in the tissue extracts and in the precipitate produced by cold from oxalate plasma is called thrombokinase.

It may be obtained not only from extracting tissues but also from stroma of red cells and from leucocytes or lymph cells. In fact the granular precipitate containing it is the blood platelets. The other substance is thrombogen and is contained only in the plasma of the blood.

The existence of this other substance, thrombogen, is denied by Howell, who considers that the prothrombin is always present in the blood, and that it immediately reacts with lime salts to form thrombin whenever the action of antithrombin is prevented by neutralization with a thromboplastic substance. In other words, the thromboplastic substance of Howell replaces the thrombokinase of other authors, and instead of participating with another body to form thrombin this other body corresponding to thrombogen is prothrombin while the thromboplastic substance corresponding to thrombokinase is active by binding or neutralizing the antithrombin. In any case, in addition to fibrinogen, prothrombin and lime salts another body formed when blood is shed is needed. The new body, according to Howell, binds the antithrombin, which in the circulating blood prevents the formation of thrombin from prothrombin in the presence of lime salts.

It has been mentioned that blood platelets are absent from birds' blood and consequently the thrombokinase. It is for this reason that birds' blood will only coagulate when allowed to come into contact with the tissues.

The Source of the Thrombokinase—The crucial step, then, in the process of clotting is the liberation of the thrombokinase in the form of the blood platelets, but we have seen that very strong reasons exist that these elements do not exist as such within the blood. Can they come by the rapid disintegration of leucocytes? It does not seem probable, inasmuch as these can be seen alive for two or three days in oxalate plasma. We must, therefore, either believe in the preexistence of the blood platelets and assume that they are elements of a most perishable character, so that the slightest contact with any other substance than the normal endothelium of vessel wall will cause them to disintegrate or, and this is more probably the correct view, that the blood platelets are formed at the time of injury to the wall of the blood vessels and the contact of the plasma with a foreign substance; that they are merely a precipitate of thrombokinase, first presenting evidence of organiza-

tion after precipitation, but rapidly undergoing disintegration.

Explanation of the Failure for Clotting to Occur within the Vessels—*Inhibition of Clotting within the Vessels*—Closely related to the crucial factor in clotting, the liberation of the thrombokinase, is the question of why is this substance not liberated within the vessels.

Only one answer is possible, namely, the nature of the surface forming the walls of the vessels. The walls of the vessel act in some manner which prevents the precipitation of thrombokinase or thromboplastin, possibly by a secretory activity of the endothelial cells themselves or in virtue of the physical characters of the lining endothelium itself.

The following facts indicate that the nature of the surfaces of the walls of the vessels, aside from any secretory activity on the part of the endothelial cells constituting them, is an important factor in the failure of thrombokinase to be liberated from the plasma within the vessels.

The fact that blood will remain for so long fluid if received into dust-free paraffin or oil tubes.

That birds' blood may be made to coagulate even if drawn without contact with the tissues, if after drawing it is subjected to much trauma by violently whipping it or filtering it through a clay cell. Evidence, however, exists that a mechanical insult is not the only factor in the prevention of clotting within the vessels. Under certain conditions blood serum can be shown to have a strong inhibitory effect on thrombin.

We know that leucocytes and red cells are being continually destroyed within the body. What, then, becomes of the thrombokinase in them. The circulating blood, therefore, must possess some means of neutralizing thrombokinase or thrombin. This conclusion is further confirmed by the fact that the injection of thrombin or thrombokinase within limitations into the blood stream will cause no clotting. We must, therefore, assume the presence of antithrombin or antikinase and, on account of the rapidity with which it must be formed, that it is produced by the endothelial cells of the vessels themselves. Intravascular clotting can be produced if very strong solutions of thrombin are injected into the vessels.

The Nature of Thrombokinase—Normal saline extracts of tis-

sues rich in cells, such as the thymus or lymph glands will cause intravascular clotting, even the alkaline solution of the acid gastric digest of these tissues will cause intravascular clotting. These tissues contain nucleo proteins and are rich in phosphorus and contain much lecithin. The precipitated acid gastric digest contains as much as 25 per cent. of lecithin. The view that intravascular prevention of clotting is due in part to the formation of antithrombin is further strengthened by the fact that injections of small amounts of thrombin or the injection of large amounts in small doses actually diminishes the coagulating power of the plasma. Repeated injections may actually annul the coagulability of the blood. This result is exactly what one would expect from the known principles of immunity, assuming that the prevention of intravascular clotting depends upon the production of antithrombin.

Metathrombin—Not all the thrombin is used up during clotting. Much still remains in the serum; and can be demonstrated by the usual test with a solution of fibrinogen. Thrombin, however, rapidly disappears so that in two or three days no traces of it may be found in the serum. We know that it has been transformed, because such serum can be reactivated by the addition of acid or alkali. The transformed product has been called metathrombin. It has been suggested that the metathrombin may merely be a combination product of thrombin and that the action of acid or alkali simply serves to break up this combination.

Thrombin itself is very stable, resisting the temperature of boiling water for limited periods. Its solutions may be evaporated to dryness and heated to 135° C. without destruction of the thrombin.

Explanation of How Clotting Is Prevented by the Various Means Mentioned According to the Above Theory of Clotting—*Cooled plasma* simply precipitates the thrombokinase. Sodium sulphate inhibits coagulation merely by the presence of an excess of salt. It will coagulate on dilution.

Magnesium sulphate plasma will coagulate on dilution, but not if it has been centrifuged after standing for 24 hours. It slowly precipitates thrombokinase.

Sodium Florid Plasma—Sodium florid precipitates the calcium

salts, but also carried down, entangled with the lime salts, thrombogen.

Herudin plasma acts like an antithrombin. It preserves quantitive relations.

Peptone plasma stimulates within the vascular system in antibody to coagulation.

Transudates do not clot, but can be made to clot upon the addition of thrombin or the washings of a blood clot. Transudates do not contain thrombokinase or thrombogen.

ESTIMATION OF THE BLOOD AND ITS CONTENT

Methods of Estimating the Total Quantity of Blood—A small sample of blood must be subjected to hemolysis by dilution with 100 volumes of water. This serves as a sample. The animal is then bled and minced in known quantities of distilled water and the minced products washed with the same. By a comparison of the two standards the total amount of hemoglobin is estimated. The dog contains 7.7 per cent. of weight in blood. The average amount of blood in man is 4.9 per cent. of the body weight, and in fat people may be only 1/30 of the body weight.

The figure 1/13 obtained from bleeding criminals is probably far too high. Haldane has devised a method for estimating the total quantity of blood by estimating calorimetrically from a sample of blood the amount of carbon monoxid which this sample contains in an individual who has inhaled a known quantity of carbon monoxid gas. The saturation of hemoglobin with oxygen is first determined. The experimenter then knows the percentage amount of hemoglobin which has been saturated with carbon monoxid, and from the known amount of gas absorbed the absolute amount of carbon monoxid hemoglobin formed. If he then knows the percentage of hemoglobin originally present in the individual's blood he is in a position to calculate the total quantity of blood.

Causes Varying the Total Quantity of Bloods—The total amount of the blood varies with the blood pressure. Any lowering of the blood pressure causes fluid from the tissues to pass in the blood. It may even be diluted to 50 per cent. by this process. It varies with the oxygen tension of the air breathed and, therefore, is less in high altitudes.

Estimation of the Total Number of Corpuscles—Estimation of

the number of corpuscles and amount of plasma. The corpuscles may be counted in specially ruled chambers adapted for use under the microscope and made for the purpose. The volume of the corpuscles is 50 per cent. of that of the blood.

Estimation of the Plasma by Centrifuging the Blood—The amount of plasma may be determined by subtracting the protein of the blood corpuscles from the amount of protein of the whole blood.

Estimation of the Oxygen—The oxygen content of the blood may be estimated by disassociating the oxygen of laked blood by potassium ferrocyanid and reading off the amount in cubic cc. of gas.

Estimation of the Specific Gravity of the Blood—The specific gravity of the blood may be measured by dropping a drop of blood into different dilutions of glycerin and water until a dilution is found in which the drop will neither float nor sink. It varies in man from 1057 to 1066. In woman from 1054 to 1061. The specific gravity of the serum is 1028 to 1032 and of the corpuscles 1090.

The Reaction of the Blood—The blood is alkaline and may be measured by titration against a decimal solution of sodium hydrate. It amounts to .2 gram of sodium hydrate per 100 cc. of blood. In laked blood the alkalinity is twice as much.

The degree of alkalinity depends on the indicator used. The only accurate method is to estimate the number of free ions by an electrical method. It is found to contain very few more OH ions than water. Litmus gives a fairly accurate estimation of the relation between the reaction of the blood and its carbon dioxid carrying power. This power is in proportion to the alkalinity to litmus.

Osmotic Pressure of the Blood and Corpuscles—The osmotic pressure of the blood is a most important physical character of the blood. Upon it depends in a large measure the variation in exchanges between the blood and the tissues. The pressure may be estimated by determining its freezing point. In the human being normally this is 0.56. The corpuscles and laked blood possess the same freezing point.

Constancy of the Salt Content—The conductivity of the blood is determined solely by the ions which it contains and, therefore, by the proportion of disassociated salts contained in it.

PLASMA, 486.98 grams.

Water	439.02 grams
Fibrin	3.93 "
Albumen, etc.	39.89 "
Inorganic salts	4.14 "

	Grams.			Grams.
Chlorin	1.722	=	Sulphate of potassium	0.137
Sulphuric acid	0.063		Chlorid of potassium	0.175
Phosphoric acid	0.071		Chlorid of sodium	2.701
Potassium	0.153		Phosphate of sodium	0.132
Sodium	1.661		Sodium carbonate	0.746
Phosphate of calcium	0.145		Phosphate of calcium	0.145
Phosphate of magnesium	0.106		Phosphate of magnesium	0.106
Oxygen	0.221			
	4.142			4.142

THE CIRCULATION

The Mechanism by Which the Blood Reaches the Tissues.—In order that the blood may perform its functions a system of closed tubes permeating the whole body has been developed. The important features of this system embrace not only the tubes themselves but a central pump, the heart, and a definite length of very minute vessels, the capillaries, possessing thin walls, permitting diffusion through their walls and ramifying every portion of every tissue. Thirdly, there is a delicate mechanism for controlling the pressure of the blood and the amount in different portions of the vascular system.

The Various Classes of Substances Which the Blood Transports.—The chemical substances with which it is necessary to supply the tissues may be divided into two kinds, (1) oxygen or the active agent of combustion, and (2) building material or combustible substances.

The two varieties of substances must be obtained from entirely [illegible] and organs. The oxygen is taken into the body [illegible]. The building material must undergo com- [illegible] the organs of digestion.

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The Three Kinds of Vessels—For the performance of these functions a special set of minute vessels having very thin walls and called capillaries is needed. In the human body, with the exception of the set of capillaries devoted to the taking in of oxygen, these sets of capillaries are all branches of a main vessel or artery coming off from the central pump. From the various sets of capillaries with one exception the blood is returned to the heart by a common system of branched tubes, the veins, before reentering the circulation. They thus constitute in part separate complete circuits, though with the exception of the brain, kidney and heart anastomoses with neighboring branches is frequent.

The one exception to this manner in which the blood is returned to the heart is the portal circulation, in which two sets of capillaries are in series with the arteries supplying the system and interposed between it and the veins, returning the blood to the heart.

The Peculiarity of the Oxygen Receiving Portion of the Circulation in Man, Fish, and Amphibian—The set of capillaries devoted to the intake of oxygen in man is a part of an entirely separate system originating in the heart and ending in the heart. Thus all the blood in the body must traverse the pulmonary circulation before it can reach the rest of the body.

The union between these two systems, the oxygen system and the reconstructive system, is through the heart, which, therefore, in man is really a double communicating pump. In fishes the heart is only a single pump, there being but one auricle and one ventricle. All the blood passes through the gills, where the oxygen is taken up before it reaches the rest of the body.

From these gills it passes directly to the systemic circulation. We may speak of the gills in fishes as connected up in series in the same manner as the portal circulation in man.

The fish's heart represents the primitive type of heart. Amphibia (frogs) represent a stage of development between the fish's heart and man's heart. There are two auricles and one ventricle.

The oxygen circulation leaves the heart by a common vessel with the systemic circulation, but returns by a separate vessel to the ventricle through a separate auricle.

THE CIRCULATION

STRUCTURE OF THE BLOOD VESSELS

The structure of the large arteries, of the arterioles and of the veins differs and this difference corresponds to a difference in function.

The Structure of the Arteries—All arteries possess relatively thick walls composed of muscular, elastic and fibrous tissue. In the largest arteries there is a greater amount of elastic tissue in proportion to the amount of muscular tissue than in the small arteries.

The function of the large arteries is chiefly one of conduction, to receive the blood from the heart and to pass it on. Their walls are elastic and resisting. They are never called upon to diminish to any degree in caliber. For this reason yellow elastic tissue is a far more important component in them than muscular tissue.

The Structure of the Smaller Arteries—The smaller arteries, on the other hand, are often required to undergo marked contraction; one of the most important means which the body possesses of controlling blood pressure is by this contraction. Their coats, therefore, are well supplied with muscle. Their internal coat is called the intima. It consists of a layer of endothelial cells resting upon a basement membrane of yellow elastic tissue. External to this coat is a middle layer, the media. It is thick and composed entirely of unstriped muscular fibers arranged in both a circular and longitudinal layer. The third and most external coat is called the adventitia. It is composed chiefly of white fibrous tissue with a few elastic fibers. From the very smallest arterioles the elastic tissue disappears altogether. The wall consists entirely of endothelium and muscle tissue.

It is the practically sole function of the veins to conduct the blood. Because of the usual intravascular pressures within them it is only necessary, therefore, that their walls should be capable of a small increase of blood pressure. Corresponding with this demand upon them, their walls are composed almost entirely of white fibrous tissue, and they fulfill a subsidiary reservoir-like function of storing a greater or smaller proportion of the circulating blood.

An increase of only 1 or 2 mm. of Hg. will cause an increase in the capacity of the veins of 50 per cent., and 60 mm. of Hg. will completely distend them. (Fig. 10.)

On the other hand, it will require 80 mm. of Hg. to cause a 50 per cent. distention of the arteries and a pressure of 130 to 160 mm. to completely distend them.

The total sectional area of the branches of the arteries and veins is greater than that of their parent vessels. This increase in section area is most marked in the transition from the arterioles and venules to the capillaries. The total sectional area of the capillaries is 800 times that of the aorta.

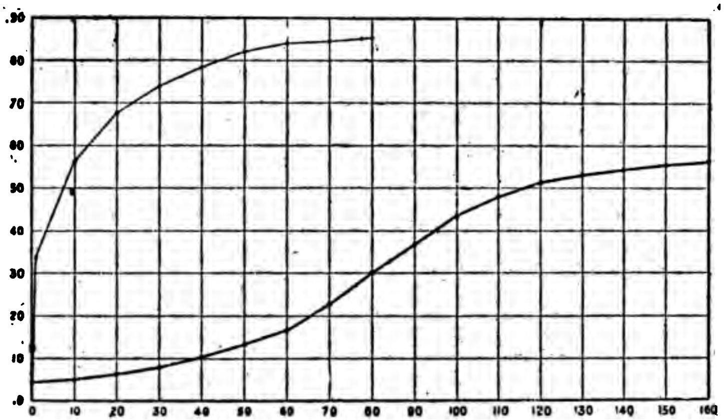

Fig. 10.—Curves of Distensibility of an Artery (Thick Line) and of a Vein (Thin Line).

The figures at the left side of the diagram represent the capacity of a section of the vessel when distended under a certain pressure, expressed by the figures on the base line in mm. Hg. (Starling.)

The impulse of the heart beat is forcible enough to cause the blood to spirt from a divided artery in jets at intervals corresponding to the heart beat.

The jet-like character of the spirt is less marked in hemorrhage from the smallest arteries, partly because of their size and distance from the heart and partly because of the resistance offered to the impulse from the heart by the elasticity of the walls of the vessels. The impulse from the heart beat does not transmit itself through the capillaries. From a divided vein the blood does not spurt, but merely flows out in a continuous stream.

By tying into an artery a cannula which is in series, by means of a solution of sodium citrate, salt and carbonate isotonic with the blood, with a mercury manometer we may record the blood

pressure and pulse changes. The record is made upon a revolving disc called a kymograph by means of an aluminium scratcher floating up and down upon the surface of the mercury in the manometer.

THE BLOOD PRESSURE

The normal blood pressure in the arteries is about 120 mm.; in the capillaries it is 20 to 40 mm. Hg. and in the veins not more than 1 to 2 mm. of Hg. In the large veins near the heart the blood pressure may be negative. The inertia of the instruments causes much deformity in the record of blood pressure curves taken in this manner. This deformity may in a large measure be prevented by a tracing made from a delicate tambour protected by a thick rubber reducing bulb, as in Erlanger's, Hurthle's or Frank's sphygmograph.

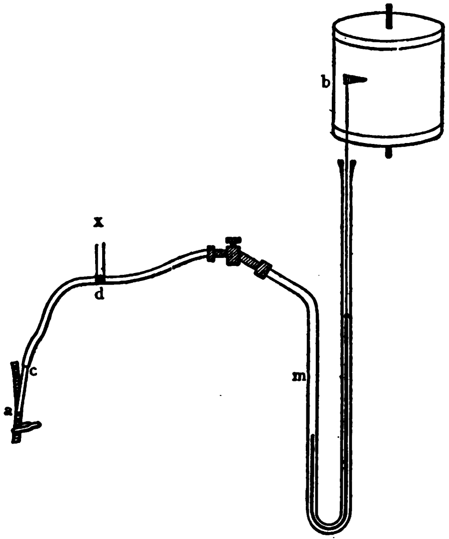

FIG. 11.—ARRANGEMENT OF AN APPARATUS FOR TAKING BLOOD PRESSURE TRACING.

a, Artery (carotid); c, cannula; d, threeway cock; m, mercurial manometer; b, drum covered with smoked paper; x, tube to pressure bottle. (Starling.)

The General Character of the Curves and the Pressures Which *They Represent*—*Using* any of these instruments, it will be observed

that the curve representing the blood pressure rises and falls with each beat of the heart. The lowest portion of the curve records the diastolic pressure and the highest point the systolic pressure. The average between the two is the mean pressure. The range between the two is known as the pulse pressure. In man the systolic pressure is 120 mm. of mercury, the pulse pressure is about 45 mm., and the diastolic pressure is about 75 to 85 mm.

Method of Measuring the Arterial Blood Pressure in Man—The arterial pressure may be measured in man by compressing the brachial artery by means of a distensible rubber cuff, fitting around the upper arm and protected by a leather cover. The interior of the rubber cuff is connected with a manometer and the cuff is distended until the brachial artery is obliterated. This point is determined by feeling for the disappearance of the radial pulse. (Fig. 11.)

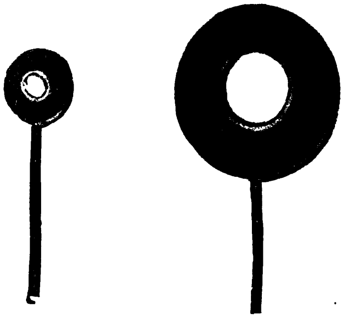

FIG. 12.—CIRCULAR RUBBER BAGS, CAPABLE OF INFLATION, FOR TAKING VENOUS OR CAPILLARY BLOOD PRESSURE.

Method of Measuring the Venous Pressure—The venous pressure may be estimated by compressing a vein beneath a circular rubber bag, which is also connected with a manometer, and gradually distending the same.

The obliteration of the vein is observed through a glass covering the hole in the center of the bag, which at the same time offers resistance to the bag as it is distended. (Figs. 12 and 13.)

The Location of Greatest Fall in Pressure in the Circulation—The fall of blood pressure between the veins and arteries is due to the fact that the arterioles possess relatively small openings and *empty their contents* into the veins, the walls of which are easily

ucts and the modification of the substances in the blood or the addition of specific chemical substances which stimulate or control functions in the body.

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The oxygen circulation leaves the heart by a common vessel with the systemic circulation, but returns by a separate vessel to the ventricle through a separate ar

distensible, so that they offer practically no resistance to the flow of blood through them. To a certain extent it is as though the capillaries emptied into a large flaccid, reservoir-like bag.

The location of the various places of greatest fall in pressure within the circulatory system is determined by the sites of greatest resistance to the current of blood.

A Mechanical Arrangement Reproducing the Pressure Relations of the Various Portions of the Circulation—The whole question is best understood by comparing the circulation to a reservoir of infinite size which communicates at its bottom with a horizontal tube of uniform bore and from which at regular intervals a series of perpendicular pipes arise. (Fig. 14.) As the water flows out of the reservoir through the distal opening of the horizonal pipe it will occupy at any one time different levels in the upright tubes. The height of these levels will all be in the same straight diagonal line. It will be possible, in other words, to draw a straight diagonal line across the top levels of the water in the upright tubes.

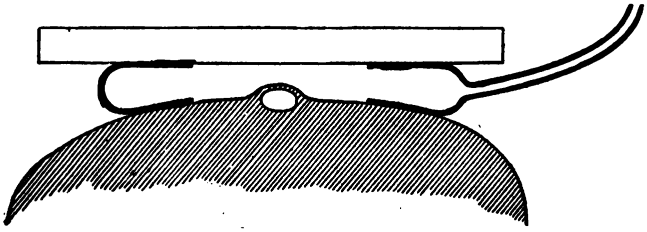

Fig. 13.—Same Rubber Bag as in Fig. 12, Shown in Cross Section, as Applied Over a Vein and Covered with Glass, Through Which the Degree of Pressure Necessary to Obliterate the Vein May Be Determined.

This line, however, will not cut the reservoir at its top, but at a distance below the surface of the water within it. This distance will represent the head under which the water flows out of the pipes.

If we introduce at any point between the upright pipes a stopcock, by which the resistance to the flow of water through the horizontal tube may be increased, one straight diagonal line will not connect the level of the water in the upright pipes on both sides of the stopcock. Two lines are now required. On each side of the stopcock a separate straight line will connect the levels of

the top of the fluid and the line on the proximal side will be higher than the line on the distal side. The level of the water in the upright pipes, which are proximal to the point of increased resistance, will be higher than in those pipes distal to it. (Fig. 15.)

The effect of the increased resistance at the stopcock represents the effect of the increased resistance offered by the arterioles and the capillaries to the circulation of any fluid through a closed system of tubes, and may be used to demonstrate that the velocity of the circulation is proportional to the pressure and inversely as the resistance.

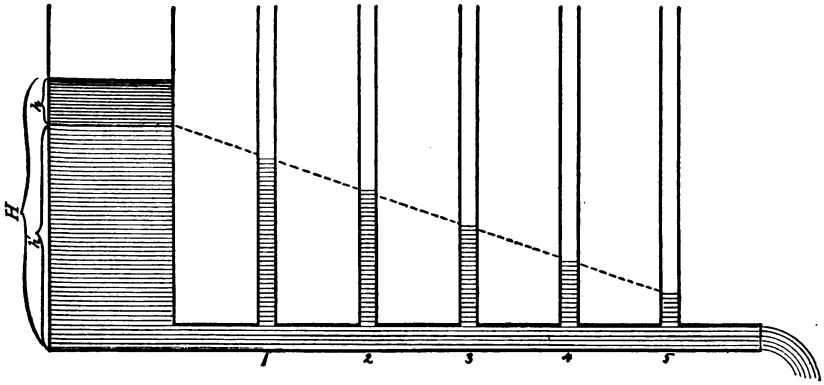

FIG. 14.—SCHEMA TO ILLUSTRATE THE SIDE PRESSURE DUE TO RESISTANCE, AND THE VELOCITY PRESSURE. (Tiegerstedt.)

H, A reservoir containing water; 1, 2, 3, 4, 5, the outflow tube with gages set at right angles to measure the side pressure; h', the portion of the total pressure used in overcoming the resistance to the flow; h, the portion of the total pressure used in moving the column of liquid—the velocity pressure. (Howell.)

$$V = \frac{L\,P}{R}$$

In this illustration the reservoir furnishing the constant pressure under which the fluid flows through the pipes represents the heart. The stopcock represents the resistance offered by the arterioles and the difference in pressure on its two sides the difference between the arterial and venous pressure. If the stopcock is opened widely the water will quickly run out of the reservoir and *the pressure* on the two sides of the stopcock become equal. The *circulation within the* body differs from this crude mechanism in

that it forms a close circuit beginning and ending in a central pump, the heart. Nevertheless, the resistance offered by the veins to the collection of blood within them and the power of the heart to pass out from itself all the blood brought to it by the veins creates conditions resembling those in the mechanism in so far that when the arterioles dilate the blood tends to flow out from the arterial side of the circulation into the venous side. The power of the arterioles, of maintaining a certain favorable degree of constriction, permits of the blood, as it is returned to the heart by the veins, being piled up on the arterial side of the circulation at a pressure relatively high to that in the veins. It will be appreciated at once that in such a closed circuit operating for the maintenance of this favorable distribution of the blood two other factors are of equal importance to the degree of constriction in the arterioles. One of these is a steady supply of blood to the heart by the veins and the other is a favorable strength of heart beat. If a certain portion of the vascular system unduly dilates, an abnormal quantity of blood will be stored up in this dilated portion and prevent the return of a favorable quantity to the heart. Inasmuch as the central pump or the heart cannot give out more than it receives, if it *receives an insufficient* quantity, it will give out too little blood to *keep the pressure high on the* proximal side of the arterioles, i.e., on

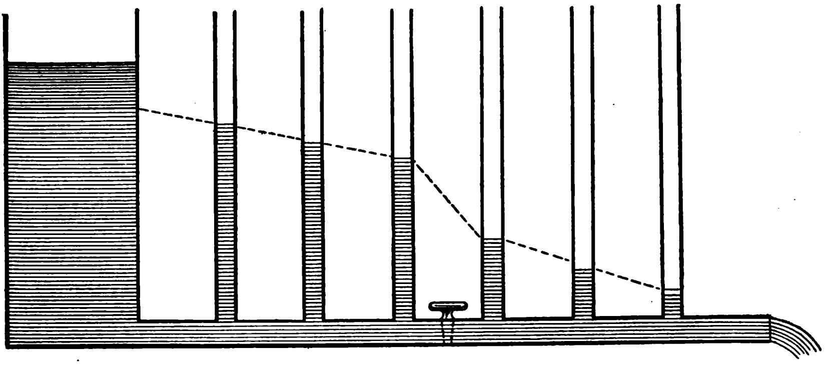

FIG. 15.— SCHEMA LIKE THE PRECEDING, EXCEPT THAT A STOPCOCK IS INSERTED AT THE MIDDLE OF THE OUTFLOW TO IMITATE THE PERIPHERAL RESISTANCE OF THE CAPILLARY AREA.

The relations of internal pressure on the arterial and venous sides of this special resistance is shown by the height of the water in the gages. (Howell.)

the arterial side of the circulation. If, on the other hand, the central pump beats too freely or stops, blood will run out through the arterioles, however much constricted, and soon the pressures on both the proximal and distal sides of the arterioles will become equal.

The Site of the Greatest Fall in Pressure in the Circulation—The distribution of the different blood pressures in circulation throughout the various vessels of the vascular system demonstrates that the greatest change in resistance to the current of blood is situated in the arterioles. (Fig. 16.)

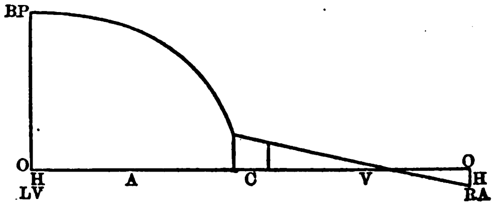

FIG. 16.—SCHEME OF BLOOD PRESSURE.

A, In the arteries; C, in capillaries; and V, in veins; OO, line of no pressure; LV, left ventricle; RA, right auricle; BP, height of blood pressure. (Starling.)

The total sectional area of the arterioles, while greater than that of the arteries, is much less than that of the capillaries, whereas the difference in the diameter of the arterioles and capillaries amounts to very little.

The fact that the greatest resistance to the flow of blood is offered by the arterioles may be shown by an experiment which increases their diameter, as, for instance, a division of the upper part of the spinal cord. The increase in the diameter of the arterioles thus produced will reduce the blood pressure one-half.

The Relative Pressures in the Various Arteries, Veins and Capillaries—The following are the blood pressures in the various parts of the circulation:

Large arteries (carotid), 90 mm. Hg. (65–110).
Medium-sized arteries (radial), 85 mm. Hg.
Capillaries, 15 to 40 mm. Hg.
Small veins of the arm, 9 mm. Hg.
Portal vein, 10 mm. Hg.

Inferior vena cava, 3 mm. Hg.
Large veins of neck and chest, 0 to —8 mm. Hg.

The Relation of the Rapidity of the Circulation to the Needs of the Tissues—Inasmuch as one important function of the blood is to supply the tissues with oxygen and nutritive substances and to remove from them waste products, any diminution of the quantity of the blood passing through the capillaries, below a degree which is sufficient for the need of the tissues, will impair the activities of the cells of the body. A diminution of a favorable quantity of blood within capillaries will be brought about by any diminution in the rapidity with which the whole blood of the body passes through them.

The Actual Velocity of the Circulation through the Aorta, Capillaries and Large Veins—Under normal condition the velocity of blood in the aorta is about one-half a meter a second. In the capillaries it is approximately one-half a millimeter a second. The average length of a capillary is about 0.5 mm. The total sectional area of the large veins near the heart is about twice that of the aorta; the velocity of the blood through them is therefore one-half of that through the aorta. The blood remains, therefore, within the capillaries approximately one second. In this brief time the tissue must receive from the blood sufficient oxygen and deliver to it their waste quantities of carbon dioxid and other substances. The oxygen and waste products cannot, moreover, pass directly from and to the blood, but must do so through the capillary wall of endothelium and the lymph filling the lymph spaces immediately external to the capillaries and intervening everywhere between them and the tissues. Everything, therefore, related to the well-being of the tissues depends upon the velocity of the circulation through the capillaries. A clear conception, therefore, of the factors controlling the rapidity of the capillary circulation is of much importance.

An Increase in the Force of the Heart Beat—The effect of increasing the force of the heart beat upon the rapidity of the capillary circulation can readily be appreciated without further explanation.

Changes in the Caliber of the Arterioles—The effect, however, of changes in the caliber of the arterioles is far more complicated and must be considered as operating under two conditions:

1. First the effect of changes in the caliber of limited portions of the circulatory system, as, for instance, portions supplying a single organ of such a small size that dilatation or contraction of its arterial supply can have no effect upon the general blood pressure. In this instance we have to deal with only the local effects of the changes in the caliber of the vessels; a contraction of the afferent vessels diminishes the amount of blood entering the capillaries of the area or organ in question, while a dilatation produces the opposite effect. In the former case the tissues are less well supplied with blood and their function is suppressed. In the latter case the tissues are well supplied and their function is stimulated. The blood on emerging through the efferent venules may be still of a bright red color and even impart a pulsation to the veins.

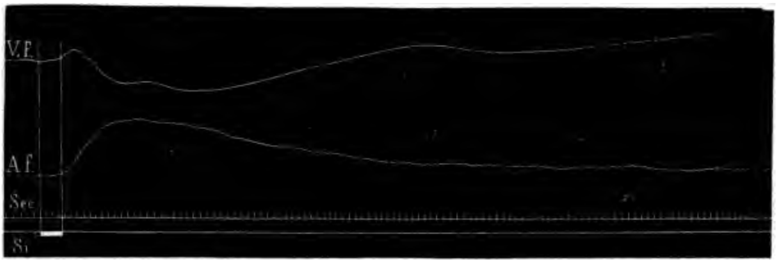

Fig. 17 Illustrates the Reversed Effects upon Arterial and Venous Pressures in the Facial Artery and Vein Produced by Stimulation of the Vasoconstrictors.

At first there is a slight rise of venous pressure due to the inflow of blood into the veins at higher pressure; then a marked fall of venous pressure, and finally the venous pressure becomes greater than at first.

V.f. = venous pressure
A.f. = arterial pressure
Sec. = time in seconds.
St. = signal marking period of stimulation.

2. Generalized changes in the caliber of the arterioles throughout the whole body or, at least, over a sufficient area to seriously affect the general blood pressure, may produce quite different effects. In order to understand the consequences of generalized changes in the caliber of the arterioles the effects of deviations from that degree of contraction which is most favorable to the needs of the tissues must be considered.

Excessive Arterial Constriction—First, what will be the consequences of a greater degree of contraction than the optimal

amount—that amount, in other words, which permits of the swiftest current of blood through the capillaries? Such a contraction will immediately cut down the amount of blood which is permitted to pass into the capillaries, and the blood retained upon the arterial side of the system will be retained at a higher blood pressure. (Fig. 17.) The increased pressure will evoke from the heart a stronger beat up to a certain degree of constriction; the increase of pressure and stronger beat of the heart will compensate for the constriction of the arterioles by forcing more blood through them than can pass through the same size vessels, under normal arterial pressures.

Beyond a certain point, however, the burden of a continued contraction of the arterioles becomes too great for the compensating power of the heart and cuts down the amount of blood entering the capillaries to such a degree that the swiftness of the capillary circulation is materially slowed.

During the unfavorable degrees of arterial constriction, though the blood pressure on the arterial side of the circulation is greatly increased, yet an excess of blood cannot be said to be stored up upon the arterial side of the system. The diminution of space on the arterial side of the system, due to the contraction of the arterioles, more than balances the effect of the increase of blood pressure upon the capacity of the arterial system. As the augmentation of the heart beat fails to compensate sufficiently in forcing the normal quota of blood through the capillaries, a time is reached when the excess of blood retained upon the proximal side of the arterioles begins to be dammed back through the heart upon the venous side of the circulation, and this condition still further diminishes the rapidity of the capillary flow.

Excessive Arterial Dilatation—What will now be the effect upon the capillary circulation of a dilatation of the arterioles?

When the arterioles dilate beyond that degree which is most favorable to the speed of the capillary circulation a large quantity of blood at first flows out from the arterioles through the capillaries and into the venules, and the capacity of the arterial side of the circulation becomes somewhat increased as a result of the arterial dilatation.

For these two reasons the arterial blood pressure becomes reduced and still further reduced because the low blood pressure

evokes a weaker beat from the heart, although the latter is, to a certain degree, compensated for by an increase in the frequency of the heart beat. In this connection it must not be forgotten that the combined sectional area of the capillaries is much greater than that of the arterioles, while the diameter of the smallest arterioles differs little from that of the capillaries. Consequently when the arterioles dilate it is as though the passage between the arterial and venous sides of the circulation was opened wide, with no resistance to oppose the rapid flow of blood away from the arterial side of the circulation and its collection within the wider bed of the capillaries and venules.

Effect of Long Continued Excessive Capillary Dilatation—The caliber of the capillaries and venules is largely dependent upon the intravascular pressures to which they are subjected, and while their walls possess a certain power of elastic contraction, the latter is only sufficient to enable them to cope with the normal conditions of the circulation and not sufficient to enable them to resist the sudden onrush of blood from the arterial side of the circulation, and particularly is this true of the capillaries and veins of the splanchnic area.

A considerable quantity of blood collects, therefore, upon the venous side of the circulation. This quantity of blood may very properly be termed the portion of the blood which holds the balance of power of the circulation, because its extraction from the arterial side of the circulation brings about such a reduction of the arterial blood pressure, by virtue of the failure of the return to the heart of an optimal quantity of blood, that after the first onrush of blood into the capillaries and venules there is a reduction of that force which drives the blood on through the capillaries and veins. A number of other conditions acting solely from the venous side of the circulation share with this reduced arterial pressure in being responsible, as long as the arterial dilatation continues, for the failure of the power of the capillaries and venules to empty the excess of blood which they contain back again from the venous side of the circulation through the heart into the arterial side. In extreme conditions after prolonged periods of reduced arterial pressure these additional factors, acting from the venous side of *the circulation,* may be efficient alone in preventing a return to

the normal conditions of the circulation even after the causes of the primary arterial dilatation have passed away.

Influence of the Special Characters of the Portal Circulation—An important factor influencing the speed of the capillary circulation, or at least maintaining a diminution of the speed of the capillary circulation after changes in the caliber of the arterioles has once occurred, is the character of splanchnic circulation. The splanchnic circulation includes the blood supply to all the abdominal organs which supply tributaries to the portal vein. This vein receives the blood from the abdominal organs, from the stomach, the intestines, pancreas, and the spleen, and instead of returning its blood directly to the inferior vena cava it breaks up into a second set of capillaries within the liver. There are, therefore, two sets of capillaries intervening between the afferent arterioles to the splanchnic area and those efferent venules which return the blood of this area to the interior vena cava. A diminished arterial blood pressure is, therefore, less able to force any excess of blood entrapped, as it were, between these two sets of capillaries than in any other portions of the vascular system.

The vascular system of the splanchnic area forms a considerable portion of the total circulation of the body, such a large proportion that an excess of blood entrapped within it is capable alone of materially reducing the general arterial blood pressure. If, therefore, a dilatation of the arterioles to this area causes an excess of blood to flow into its capillaries and venules the immediately ensuing reduction of the arterial blood pressure will be sufficient to render the general arterial blood pressure powerless to empty the distended venules and capillaries of the splanchnic area through the second set of venules of the portal circulation within the liver; and yet there will be sufficient pressure transmitted through the dilated afferent arterioles of the splanchnic area to successfully oppose any power of the tributary capillaries and venules of the portal system to empty themselves by their own contractile power. In other words, the rate at which the blood will be delivered through the capillaries of the portal vein within the liver to the inferior vena cava will be less than the normal rate, and yet the wide open arterioles of the splanchnic area will constantly keep an excess of blood within the tributary capillaries and venules of the portal vein.

The Inertia in the Elastic Contraction of the Capillaries—This condition of affairs makes clear the part played by the second factor acting from the venous side of the circulation and responsible in part for the diminution of the speed of the capillary circulation under conditions of generalized arterial dilatation.

The second factor may be termed the inertia of the contractile power of the capillaries and veins. The pressure within the veins and capillaries after an initial distention becomes progressively less the longer the time during which they are subjected to an increase of intravascular pressure. Even after short periods of distention their power of contraction in response to a diminution of the pressure under which the blood is pumped into them, inasmuch as the general arterial pressure cannot fall until they first become distended, is far slower than the readjustment of the normal arterial caliber and never adequate until the amount of blood entering these capillaries and venules becomes cut down by a contraction of the arterioles.

The reality of this inertia becomes evident after prolonged periods of distention, when even a contraction of the arterioles becomes no longer able to bring about a normal distribution of the blood within the body. One factor explaining this inertia in the contractile power of the capillaries and venules may be a certain loss of elasticity in the walls of these vessels. Unquestionably the most important factor is the loss of the compressing force normally exerted upon the capillaries and veins from without. After more or less prolonged periods of increased intracapillary and venous pressure there occurs a diminution of the thickness of the extra capillary and venous lymph space. The lymph becomes actually forced out of these spaces and the flow through the thoracic duct increased. Under these conditions a return of the capillaries and venules to their normal caliber is resisted by the failure of any force returning the lymph to the extravascular spaces and consequently by the tendency to develop a negative pressure in these spaces. The sequestration in this manner of a portion of the total quantity of blood of the body within the veins necessarily means that less blood will be received by the heart. If less blood is received by the heart, the heart in turn cannot deliver the normal quantity to the arterial side of the circulation, so that this consequence forms another seg-

ment of the train of events contributing together in a vicious circle, as it were, to keep the blood pressure low.

The Influence of the Shortened Total Diastolic Period—Still another factor must be added to these consequences. Under the conditions of lowered blood pressure the heart attempts to overcome the reduced pressure by an increased frequency of its beat. The rate of the heart is increased at the expense of diastole. Such a condition means that the total period during which the heart is receiving blood is cut down so that for this reason, even though it may only be a corollary to the fact that less blood flows to the heart, the heart is unable to deliver a normal output to the aorta.

The Influence of Hydrostatic Pressure in the Venous System—The above discussion has not considered the possible effects of hydrostatic pressure. The mechanical factors involved in the circulation of the blood have been considered upon the basis of a horizontal system of tubes. The influence of hydrostatic pressure cannot be entirely neglected. Its effects, however, become chiefly manifest, especially in the splanchnic area, under conditions of dilatation of the arterioles. Indeed, as will later be explained, it is upon the presence of valves in the veins, the extravascular pressure (muscular contractions around the veins) and chiefly the power of response of the arterioles to increase of intravascular pressure that at all makes possible a normal return of blood to the heart under conditions of vascular dilatation, including as it must an inhibition of the myogenic contractions of the arterial wall, the force of hydrostatic pressure must be added to all other factors mentioned in preventing a normal return of blood to the heart. In such an animal as a rabbit, for instance, with its very lax abdominal wall, it is said that death may result alone from suspending the animal by its ears. The cause of syncope in the human being is an inhibition of the vasomotor center, and the beneficial effects of the prone position in this condition make evident the powerful effect of hydrostatic pressure in preventing the return of the blood to the heart in conditions of vascular dilatation of the arterioles. Inasmuch as the portal vein and its tributaries have no valves and the contractions of the abdominal muscles are probably not transmitted so directly to the portal vein and its tributaries, the influence of hydrostatic pressure must be considered to be an important factor when it is added to the other factor operating through this

portion of the circulation in preventing the discharge of an excess of blood contained within it.

THE HEART CIRCULATION

THE ANATOMY OF THE HEART AND THE COURSE OF BLOOD THROUGH THE HEART.

The heart is a muscular organ containing four chambers. (Fig. 18.) Two of these chambers, the right and left ventricles, are concerned in pumping the blood into arteries, which convey the blood respectively to the lungs and to the body. The other two chambers of the heart, the right and left auricles, receive the blood respectively from the body and the lungs. The right auricle receives the blood back from the systemic circulation through the superior and inferior vena cava. The blood entering the heart through these vessels is venous blood, containing much carbon dioxid. It passes from the right auricle into the right ventricle. By the contraction of this ventricle it is forced into the pulmonary artery, which conveys the blood to the pulmonary capillaries. From these vessels it passes into the pulmonary venules and then by the four pulmonary veins to the left auricle of the heart.

The left auricle by its contraction forces the blood into the left ventricle, and from this ventricle it is forced into the aorta. The branches of the aorta carry the blood to the capillaries of every portion of the body, from which it is returned by the venules and veins and finally by the superior and inferior vena cava to the heart, whence it begins once more the circuit of the body.

The passage of the blood in only one direction through each chamber of the heart depends upon the presence of valves between the auricles and ventricles and at the entrance to the aorta and pulmonary artery.

The valves placed between the auricles and ventricles are flat or flap-like structures, composed of fibro-elastic tissue lined with endothelium. One edge is attached to the margin of the auriculo-ventricular opening. By the opposite free margin they are attached with tendinous cords to the summits of little muscular elevations projecting into the cavity of the heart from the opposite ventricular walls.

The openings to the pulmonary artery and aorta are guarded by three cup-shaped valves or pockets attached at their external periphery to one-third of the margin of the aortic or pulmonary opening. The free margin of each pocket possesses at its center a small fibro-cartilaginous nodule, the corpus Arantii.

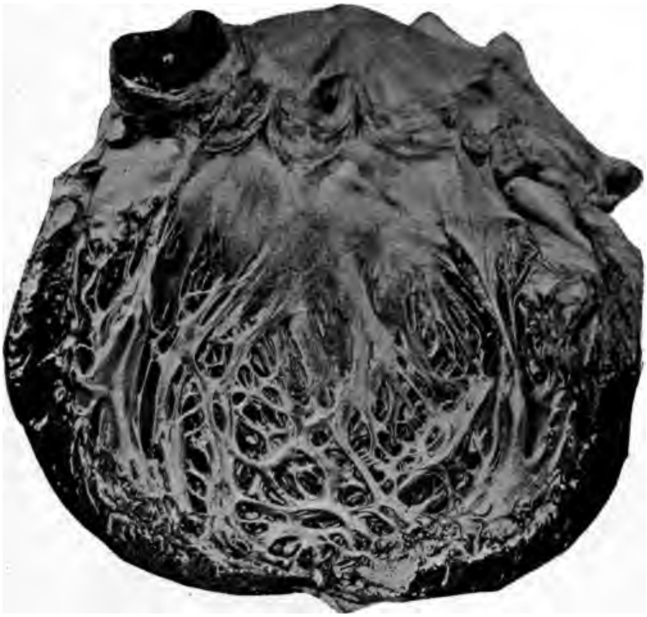

FIG. 19.—VIEW OF THE INTERIOR OF THE LEFT VENTRICLE OF THE HUMAN HEART.

The ventricle has been opened through its anterior wall between the two papillary muscles from the apex through the aortic opening. Each side is hooked back and there appears the aortic wall above laid open—separating this from the ventricular cavity are the three semilunar valves. At the upper left corner is the opening of the pulmonary artery. Attached to the tips of the papillary muscles on each side of the ventricular cavity are the cordæ tendineæ, uniting to these muscles the large flaps of the auriculoventricular valves seen just beneath the aortic opening.

Because of the shape of each pocket, these valves are called semilunar valves. When closed, the three nodules come together at their center and by their free margins. Their edges are lined with delicate endothelium, and when coapted form three lines radiating from the center. The entrances of the veins into the auricles is guarded by encircling muscular fibers, which contract around the

opening of the veins when the auricles contract and thus prevent the blood passing back into the veins.

The main cavity of the right auricle is called the sinus venosus, or the atrium; a smaller cavity comes off from this anteriorly; it is called the auricular appendix. Anterior to the opening of the inferior vena cava, a crescentic fold passes from above the caval opening to the inner wall of the auricle. There it terminates in relation with a shallow inner wall of the auricle, where it is in

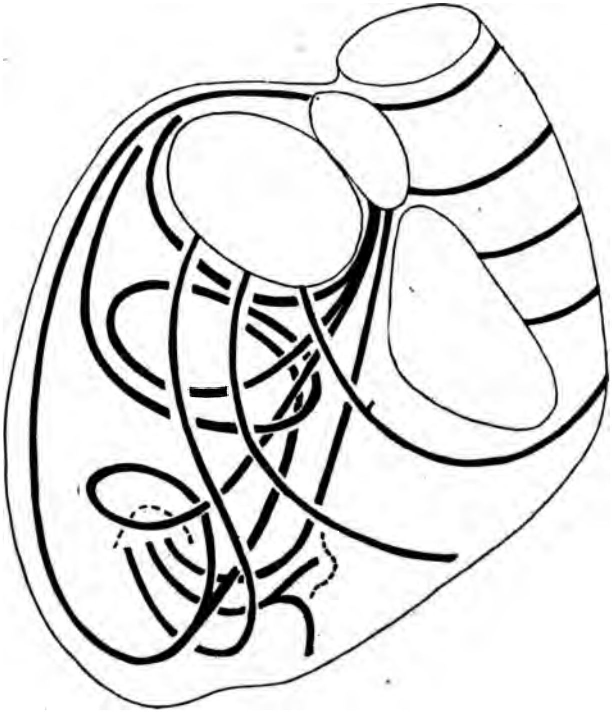

FIG. 20.—DIAGRAM TO ILLUSTRATE THE DIRECTION OF THE CHIEF MUSCULAR BUNDLES OF THE HEART SEEN FROM BEHIND.

The two auriculoventricular openings appear above in the foreground, with the opening for pulmonary artery and aorta behind. The sinospiral fibers are seen arising from the left auriculoventricular opening and sweeping around to the right around the right ventricle, while the bulbospiral sweep from the auriculoventricular ring in the region of the septum to the left, forming spiral turns around the ventricle, ending around the base of the aorta.

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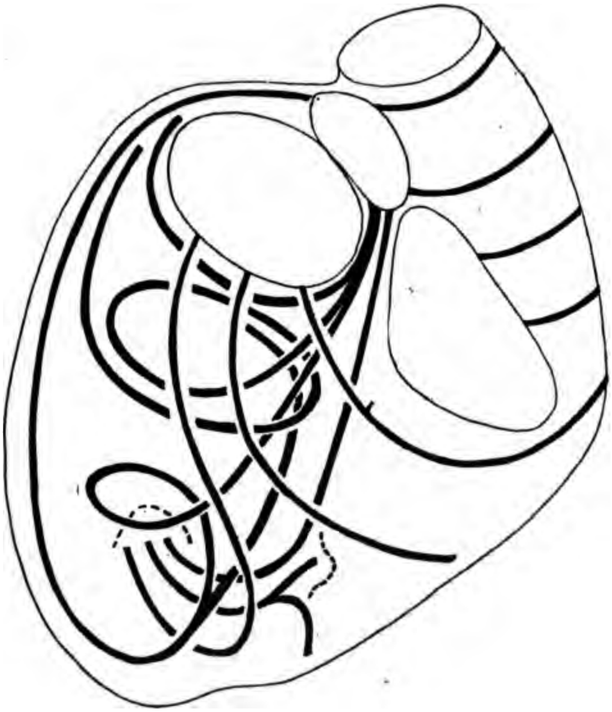

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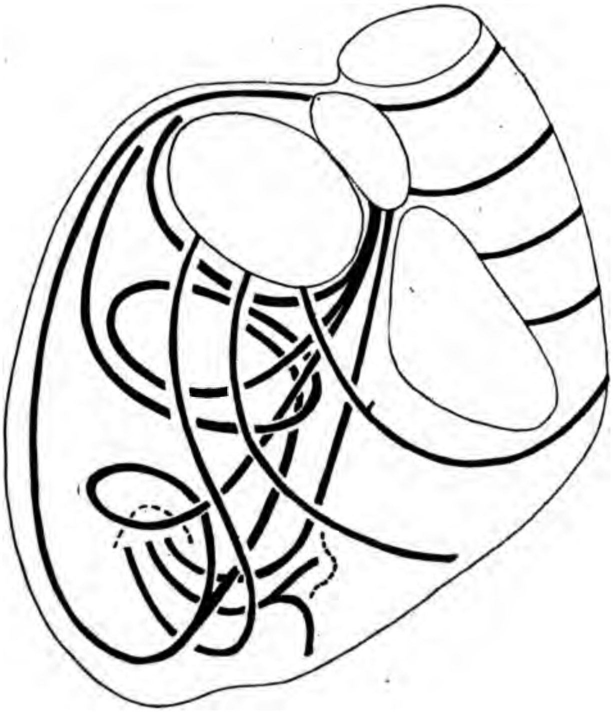

Fig. 20.—Diagram to Illustrate the Direction of the Chief Muscular Bundles of the Heart Seen from Behind.

The two auriculoventricular openings appear above in the foreground, with the opening for pulmonary artery and aorta behind. The sinospiral fibers are seen arising from the left auriculoventricular opening and sweeping around to the right around the right ventricle, while the bulbospiral sweep from the auriculoventricular ring in the region of the septum to the left, forming spiral turns around the ventricle, ending around the base of the aorta.

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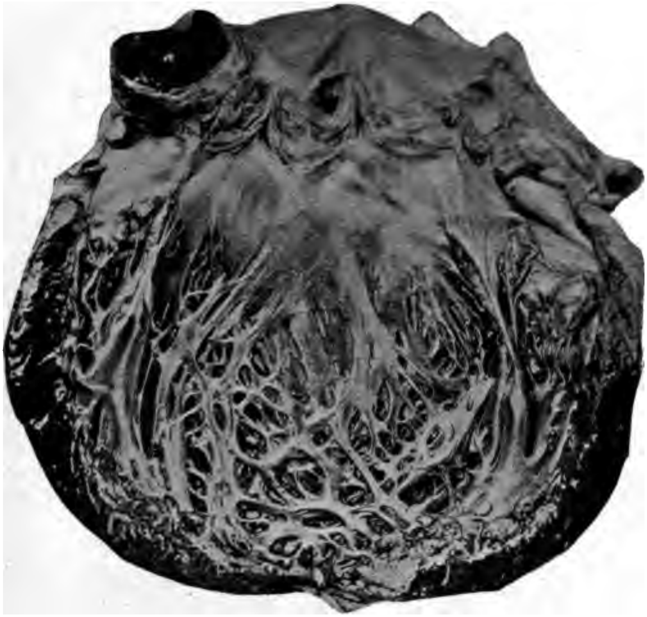

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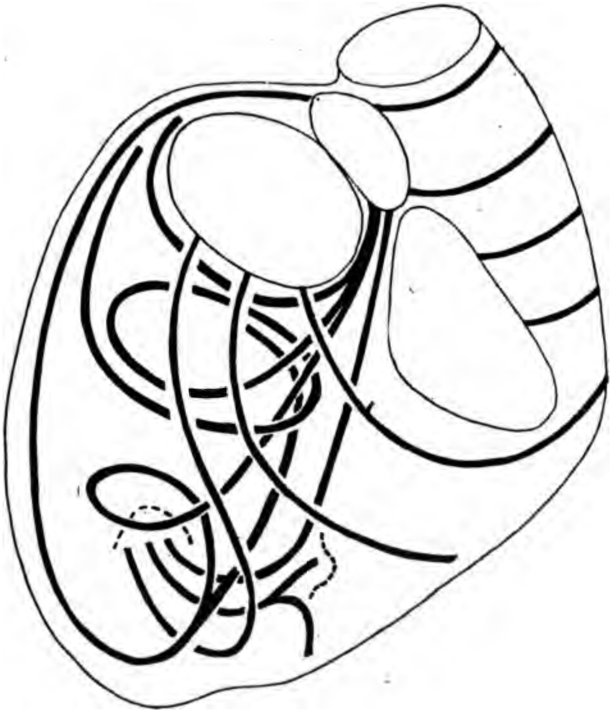

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relation with a shallow depression, the fossa ovalis. The fold is called the Eustachian valve.

During fetal life the fossa ovalis was a foramen, the foramen ovalis. It served to allow the passage of the blood from the right auricle directly to the left auricle, a short circuit, in other words, around the lungs, for which organs the fetus has no use.

Between the opening of the superior and inferior vena cava is quite an elevation, the tubercle of Lower. Between the opening of the inferior vena cava and the right auriculo-ventricular opening is the coronary sinus. Into it open the coronary veins. The coronary sinus is guarded by a vestigial valve, the valve of Thebesius.

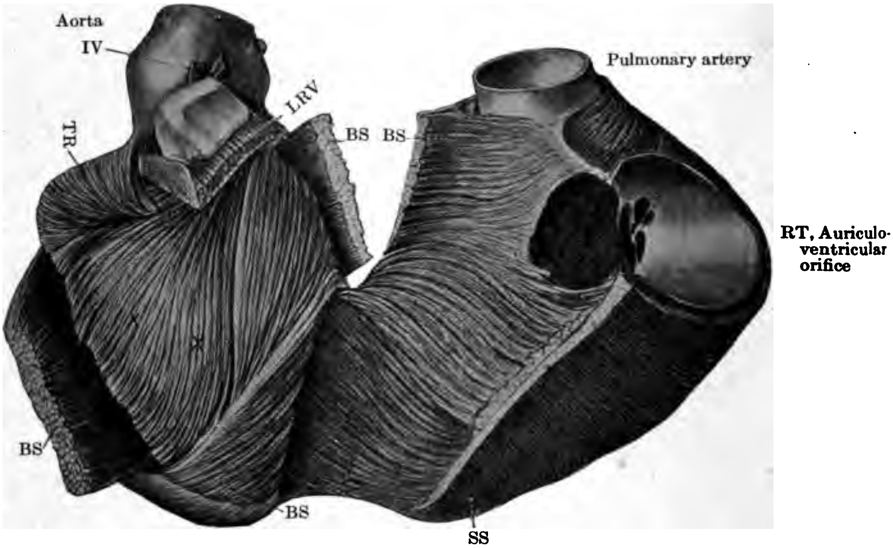


FIG. 21.—INTERIOR MUSCULATURE OF THE HEART WITH THE SEPTUM COMPLETELY DIVIDED.

BS and BS, superficial and deep bulbospiral bands; SS, sinospiral fibers; IV, interpapillary band; LRV, origin of the longitudinal bundle of the right ventricle which entered the hole torn in the right ventricle; TR, posterior triangular field; X, termination of the bulbospiral bands. (Franklin P. Mall.)

The right ventricle is somewhat crescentic in shape on cross-section. Its cavity is prolonged upward into the pulmonary artery. This cone-shaped prolongation is called the infundibulum, or the conus arteriosus; within the ventricle muscular ridges and a papillary elevation project from the walls.

These ridges are called columnæ carneæ. Instead of forming ridges, these bands may be attached at both ends only. The papillary elevations are called musculi papillares; the right ventricle contains three and the left two large ones. To their free end the chordæ tendineæ are attached. They hold down the free edge of the auriculo-ventricular valves.

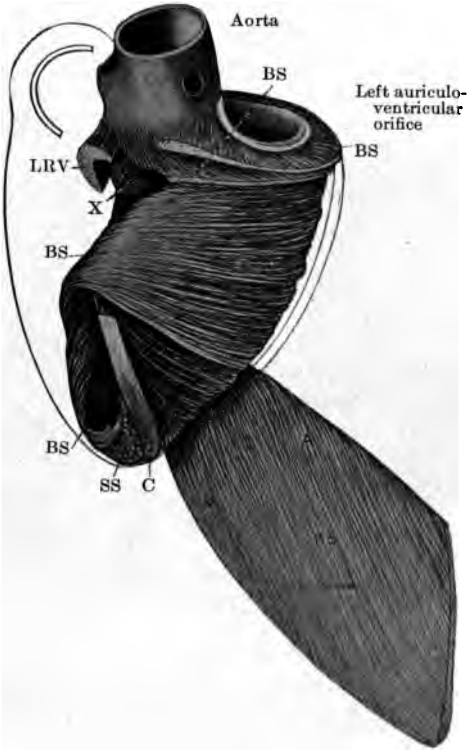


Fig. 22.—Same View as Fig. 21, with the Superficial Bulbospiral Band Thrown Back and the Deep Bulbospiral Band Exposed Entirely.

The origin of these two bundles is shown, BS and BS, at the base of the heart; C, a strand of the bulbospiral band not turned back; LRV, longitudinal bundle of the right ventricle. The course of the bulbospiral band is marked BS. It ends at X. (Franklin P. Mall.)

The special features of the right auricle are the openings of the four pulmonary veins. The left ventricle differs from the right in that a cross-section of its cavity is circular and its muscular walls are much thicker.

The Heart Muscle—The muscular layers of the heart form, roughly, a superficial and a deep set. (Figs. 20, 21 and 22.) Each of these may be divided into a set belonging chiefly to the right, the sinospiral group, and another to the left ventricle, the bulbospiral group. The superficial fibers arise from the tendinous structure of the auriculo-ventricular ring, pass obliquely down on the superficial surface of the right or left ventricle, forming, especially in the case of those belonging to the left ventricle, spiral turns around the regions of the apex of the ventricle, and then turn upwards to end in the interventricular septum, or the papillary muscles.

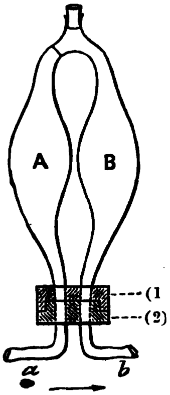


FIG. 23.—LUDWIG'S STROMUHR.

Two bulbs, A and B, fixed to the upper metal disk (1); two cannulæ, *a, b,* fixed to the lower metal disk (2); the upper disk movable round the lower, so that the connection between the bulbs A B and the cannulæ *a* and *b* can be reversed or interrupted. Cannula *a* fixed in central end of carotid, cannula *b* in peripheral end. Bulb A first filled with oil, bulb B with defibrinated blood. Blood from the central end of artery enters A, and drives by means of the oil the blood in B into the peripheral end of artery. A being full of fresh blood, B is full of oil: the position of the bulbs is suddenly reversed by a half revolution of the upper disk. B (full of oil) is now connected with *a;* A (full of blood) is connected with *b.* The maneuver is repeated several times.

Given the capacity of a bulb, the number of times it has filled and emptied, and the sectional area of the artery, the velocity of the blood current is calculated: e.g., a stromuhr placed on a carotid artery of a small dog showed a flow of 90 cc. per minute, i.e., 1.5 cc. per second. The sectional area of the vessel was 5 square mm., i.e., 1/20 square cm. The rapidity of the current is, then, 1.5 divided by 1/20, i.e., 30 cm. per second. (Waller.)

The deep fibers are mostly circular, surrounding the ventricles.

Many of them lie between the superficial and deeper portions of the superficial fibers. Those of the left side arise mostly from the base of the aorta. Those of the right side surround the conus arteriosus, and both are attached to the auriculo-ventricular ring.

The auricular muscular fibers are continuous over both auricles and ventricular fibers over both ventricles. The auriculo-ventricular ring forms a well-marked division between the auricles and ventricles. Nevertheless, a very important band of fibers, the bundle of His, forms a muscular bridge between the auricles and ventricles. It arises in the wall of the right auricle, passes beneath

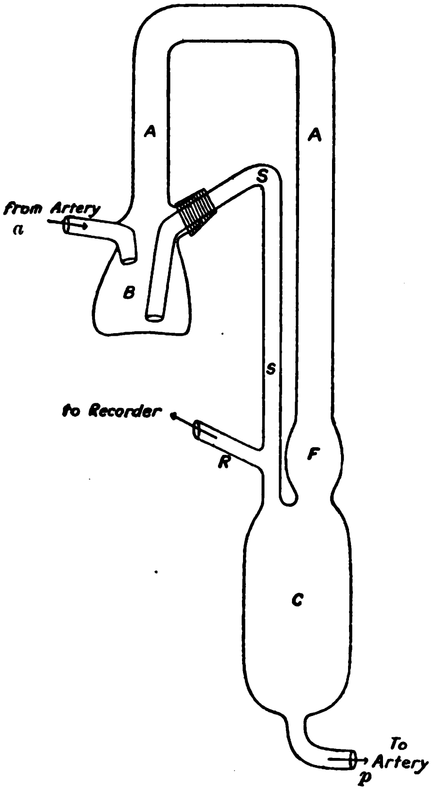


FIG. 24.—A SIMPLE BLOOD CURRENT MEASURE. (Starling.)

When B and tube A fill high enough to overflow through S, the larger limb S quickly empties the bulb B, so that it is merely necessary to count the number of times B empties per minute to know the rate of flow.

the foramen ovalis across the auriculo-ventricular juncture, to end in the interventricular septum. Provision is thus made for simultaneous contraction of both auricles and ventricles and also for propagation of impulse along a band of muscle from the auricle to the ventricle.

The Pericardium—Surrounding the whole heart is a strong sac called the pericardium. It is continuous above with the large vessels at the base of the heart and lined internally with endothelium. It possesses a definite function in controlling the degree of filling of the heart during diastole. This function can be demonstrated by opening the sac and noticing the bulging of the ventricular wall through it each time the ventricle is filled by the contraction of the auricles, provided the rate of the heart is not too rapid.

The Velocity of the Blood—The velocity of the blood is measured by counting the number of times that it will take to empty and fill stromuhrs of various shapes which are inserted in the course of arteries. (Figs. 23 and 24). Variations in its velocity may also be recorded from a delicate tambour, the lever of which is operated by a fan moved by the current. They may also be recorded by photographing the difference in the height of two columns of blood within two tubes inserted at a short distance from each other in the course of an artery. The first tube receives the blood current directly, while the second is placed at right angles to the current. During systole the velocity of the blood is greater than during diastole. In the carotid of the horse during systole it is 520 mm. per second and during diastole it is 150 mm. per second. The following table has been prepared from experiments on the dog:

			LINEAR VELOCITY			
BODY WEIGHT.	ARTERY	VOL. PER SEC.	PER SEC.	DIAMETER OF ART.	B. P.	NERVES.
	crural	0.63 cc.	128 mm.	2.5 mm.	77 mm.	uncut
14.6 kilo gr.	crural	1.69 cc.	275 mm.	2.8 mm.	88 mm.	cut
14.1 kilo gr.	carotid	1.95 cc.	241 mm.	3.3 mm.	93 mm.	uncut

In the large arteries of the human body the velocity of the blood is 1.5 meter per second.

The Cardiac Cycle—In general the cardiac cycle consists of a simultaneous contraction of both auricles lasting about .1 of a second. This is followed by a contraction of the ventricles, during

them is less than in the auricles, so that blood begins to flow from the auricles into the ventricles. This causes a rapid fall of the auricular pressure which had been raised by the entrance of blood into the auricles from the veins.

5. After .1 of a second more the cavities of the ventricle and auricle become filled with blood, and though both the ventricle and auricle remain relaxed for a much longer time, .3 of a second, the pressure slowly rises in the ventricle as well as in the auricle from the continued return of blood through the veins. A sum of these various periods, .1 plus .03, plus .04, plus .18, plus .05, plus .1, plus .3 equals .8 of one second, the total period of the cardiac cycle. Of this time the auricular systole lasts .1 of a second and the ventricular systole lasts .3. The auricles are at rest for .7 of a second and the ventricles for .5 of a second. The whole heart is resting at the same time for .4 of a second. Thus the period at which the heart is at rest is much longer than when it is active.

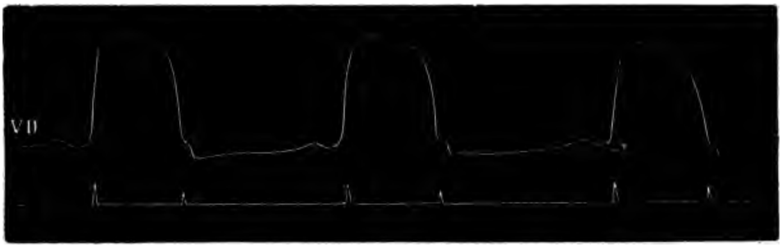


Fig. 31.—Tracing of the Intraventricular Pressure of a Horse.

On the base line the signals indicate the time of the first and second sounds. (E. J. Marey.)

When the heart action quickens it does so at the expense chiefly of diastole. Thus the pulse may vary from 32 to 124 (4 × 32) times a minute. The duration of systole for these extremes is .382 (2 × 190) of a second in the one case and .190 of a second in the second case. While then the pulse has increased four times in frequency, the systolic period has shortened only one-half.

Inasmuch as the great veins possess no valves where they enter the heart but depend upon the constriction of the cardiac muscle around their orifices for protection against the intracardiac pressure, the variations in pressure within the auricles are to a rather large degree transmitted to the veins. For each heart beat the

large veins pulsate twice. They feel the two periods of increase in the auricular pressure due to the auricular and ventricular systole.

Shape of the Heart—Changes in shape of the heart during contraction and in its relation to the chest wall:

During diastole the heart muscle is perfectly flaccid, and its shape will depend much upon the force of gravity. Inasmuch as it rests upon the anterior slope of the diaphragm, it will be flattened from before backwards and from above downwards.

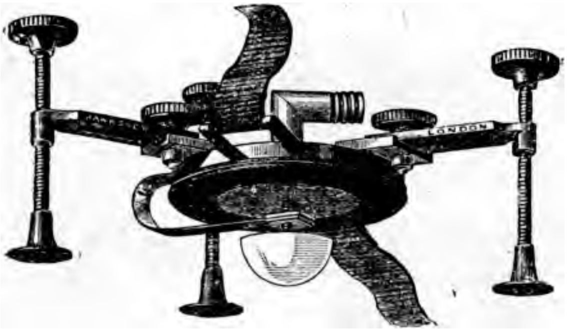


FIG. 32.—A CARDIOGRAPH.

This is strapped round the chest, the central button is applied to the "apex-beat" and its pressure on the chest wall regulated by means of the three screws at the sides. The tube at the upper part of the instrument serves to connect the drum of the cardiograph with a registering tambour such as that shown in Fig. 33. (Starling.)

During contraction the whole heart becomes rounder in its cross-section. The transverse diameter diminishes and the anterior diameter increases.

The pericardial cavity preserves the contour of the heart, and inasmuch as the pericardium is attached to the diaphragm below the apex of the heart, it is prevented from moving upwards during contraction. It will remain fixed and the base will move toward the apex. This movement can be demonstrated by passing needles through the chest wall and into the heart at its base and into the ventricle, midway between the base and apex and into the apex. During contraction the extremity of the needles external to the chest wall will indicate the movement of the base toward the apex. Neither the cavity of the right or left ventricle entirely empty themselves during systole.

Apex-Beat—Its Cause—During systole of the heart an impulse is imparted to the chest wall which can be felt in the fifth intercostal space. This impulse is generally spoken of as the apex-beat, and formerly was supposed to be caused by the apex of the heart pushing itself against the chest wall during systole.

As a matter of fact, the apex of the heart is both much lower than the fifth intercostal space and is just that portion of the heart which does not move during contraction. The impulse in the fifth space called the apex-beat is due to the anterior wall of the heart pushing against the chest wall; the antero-posterior diameter lengthens and the lateral diameter shortens in consequence of the change in shape of the heart to the cylindrical form during contraction.

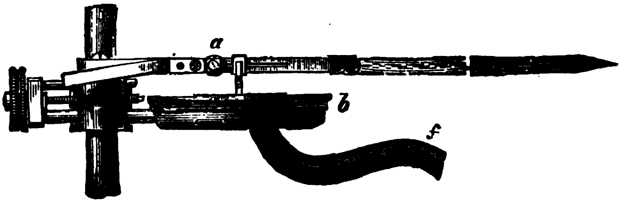


FIG. 33.—MAREY'S TAMBOUR.

a, Axis of lever; *b*, metal tray covered with rubber membrane, and communicating by tube *f* with free end of cardiac sound. (Starling.)

The Cardiometer and the Character of Its Tracings—It is possible to produce a tracing from the apex-beat which will record graphically the changes transpiring in the ventricles. An instrument for this purpose is called a cardiograph. It consists simply of a button which moves a tambour in series with a second tambour and a writing lever. (Figs. 32 and 33.) Such a tracing shows in general curves with the same characters as tracing of the intraventricular pressures. There is first a small elevation, indicating the auricular contraction, followed by the systolic wave, which slowly declines during the period of the systolic plateau until the period of relaxation of the ventricle. There is then a very rapid decline, after which the curve slowly rises again as the ventricle becomes filled with blood. (Fig. 34.)

The Three Heart Sounds—Each cardiac cycle is accompanied with two very distinctly heard sounds and a third sound described by many observers.

The relation of these sounds to the various events of the cardiac cycle can be easily studied by marking the time of their occurrence upon the tracings of the cardiac cycle. (Fig. 35.)

The first sound is a low-pitched, prolonged sound, expressed well by the word lubb. It is synchronous with the rise of pressure in the ventricles, and depends upon two causes. One of these is the closure of the auriculo-ventricular valves and the other is the muscular contraction of the walls of the ventricles. The two elements in the production of the first sound are demonstrated by the change and not the disappearance of the first sound when the large veins entering the heart are clamped so as to render closure of the auriculo-ventricular valves impossible. The first sound is heard most distinctly over the site of the apex-beat.

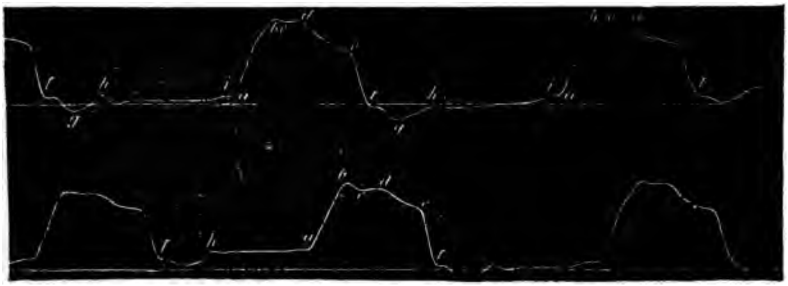


Fig. 34.—Cardiometer Tracing of the Normal Heart.

The second sound is caused by the snap back of the aorta and pulmonary valves. Hooking back these valves will cause its disappearance. Sometimes the aortic and pulmonary valves will not close quite simultaneously; we then have a reduplication of the second sound. The second sound is shorter and higher pitched than the first. It is usually imitated by the word dub. The second sound is loudest over the second right costal cartilage.

The pulmonary element is loudest over the second left costal cartilage. The third sound is difficult to hear. It is low pitched and soft. It should be listened for over the apex. It occurs a short time after the second sound during the beginning of diastole. It is caused by the first inrush of blood during diastole into the ventricles and depends upon vibrations set up in the fluid itself.

Whenever complete closure of any of the valves of the heart is

impossible because of disease which may have deformed the valves or thickened them or dilated the orifice, or whenever the orifice is contracted or changed by the production of a nodular thickening around it, vibrations will be set up in the blood as it passes through the orifices, which will give rise to a blowing bruit in place of the normal heart sound that should occur at that time in the cardiac cycle.

The Factors Responsible for the Return of Blood to the Heart—The mechanism by which the heart is filled during diastole is important. It is entirely upon the possibility of the blood flowing from the veins into the auricles that the circulation can be maintained at all. The output of the heart depends upon the quantity of blood returned to it during diastole by the large veins and, therefore, upon the pressure within these veins. With a moderate and constant return to the heart an increased arterial pressure or increased rate of heart beat does not alter the output, whereas the output of the heart is at once increased or diminished by similar changes in the venous inflow so long as the heart remains functionally capable of dealing with the increased demands upon it. The venous pressure is with these qualifications an index to the output of the heart, and there is an optimum venous pressure. Notwithstanding the relatively shorter diastole accompanying an increased

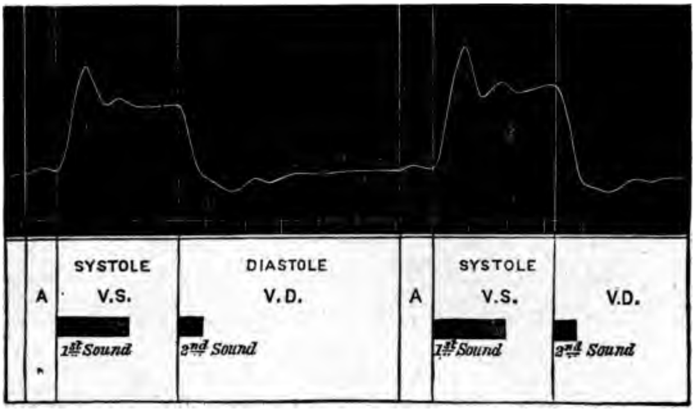


Fig. 35.—A Tracing from the "Apex-Beat" of Man.

Relation of sounds to contraction indicated below the tracing by black marks. (Waller.)

heart rate, an increase in the rate of the heart will enable the heart to deal more efficiently with maximum venous pressure, in other words, to receive and therefore expel more blood than at slower rates. The flow of blood from the veins into the auricles alone depends upon the existence of a progressive diminution of pressure between the capillaries and the auricles. The pressure within the great veins depends in turn upon the following factors:

1. Upon the blood pressure transmitted through the capillaries into the venules.
2. The position of the body.
3. The existence of valves within the veins making effectual the pressure exerted on the walls of the veins by the muscles of the body during their contraction.
4. The existence of a negative pressure within the thorax resulting from respiration.

The pressure changes in the chest are so extensive that they are quite as important as the other two causes of the return of the blood to the heart. Natural expiration is accomplished by the retraction of the lungs within the chest cavity solely as a result of their own elasticity. This retraction produces a negative pressure within the thorax at the end of expiration of 5 mm. at the end of inspiration of 9 mm. Although in forced expiration there may be an actual positive pressure created within the chest cavity, yet in forced inspiration the intrathoracic negative pressure is greatly increased. These respiratory movements produce, therefore, a pumping action upon the large veins, the walls of which are so flaccid that they readily transmit the intrathoracic pressure through them to the blood. At the end of each inspiration there is an increased flow into or storage of blood in the great veins. At the end of expiration this flow is diminished, but there is an increase in the pressure tending to drive the blood into the heart.

In extreme muscular exertions with the glottis closed a constant positive pressure may exist in the thorax which is capable of altogether stopping the return of blood to the heart. It is possible to stop the pulse at the wrist by experiments of this kind.

The Cardiopneumatic Movements—The heart in its turn also effects the intrathoracic pressures. Contracting at each systole, the space within the chest which it occupies is smaller, and consequently a diminution of the intrathoracic pressure results. These

cardiac variations of the intrathoracic pressure may be recorded in tracings of the respiratory movements taken from a delicate tambour attached to the nostril. They are called the cardiopneumatic movements. Any increased pericardial pressure diminishes the return of blood to the heart and, therefore, embarrasses the heart's action.

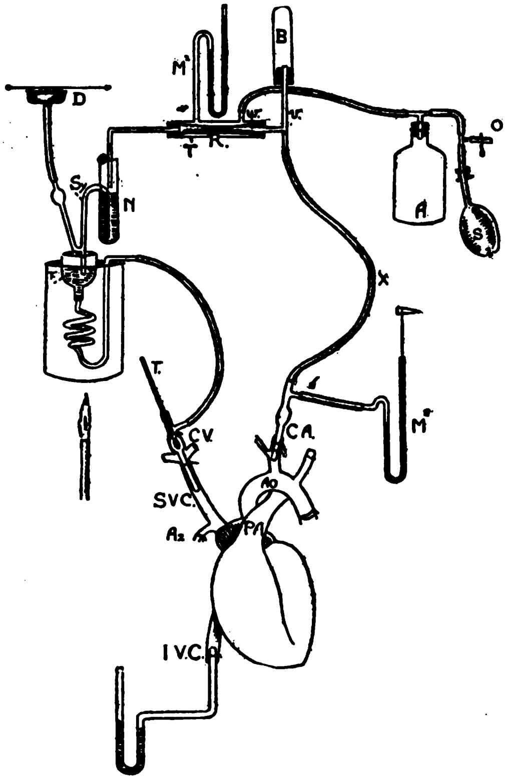


Fig. 36.—Device for Determining the Work and Output of the Heart. Cannulæ are placed in the innominate artery and superior vena cava. Between these two vessels the blood mixed with hirudin circulates at a pressure measured by the manometer, M, through the peripheral resistance, R, which can be varied by the air bulb S. The inverted air chamber, B, replaces the elasticity of the arterial walls. The blood then flows at low pressure into N. The siphon tube S can be so arranged that 10-30 cc. can be siphoned off at regular intervals. The blood is returned to the heart from the reservoir F in which it is warmed.

The Output of the Heart and Its Estimation—By a number of ingenious devices (Fig. 36) it has been possible to create an artifi-

cial circulation, using the normally beating heart as the pump, and not only registering the pressure, but also the output. These devices are called cardiometers. Another type of these same instruments incloses the heart and records the variations of air pressures produced by the cardiac contractions within the inclosing sphere and thus measures the output per beat.

As a result of experiments with these instruments the output of the right or left ventricle, for they are both equal, is from 50 to 100 c. c. at each beat. Its average output may be said to be 60 c. c.

The Work of the Heart—If the average output of the heart is 60 cc. and if the average pressure against which the heart pumps is 100 mm. of Hg. and if the velocity in the aorta during systole is 500 mm. a second, the work done by the heart during the brief period of ventricular contraction of a little less than .3 of a second would be 60 by 0.100 by 13.6, equal 81.6 grammeters. This figure neglects the factor of varying resistance in the aorta and the additional energy required to get up speed in the aorta. Both these factors are small and may be neglected. The work done in the right ventricle at each beat is 16 grammeters, the pressure in the pulmonary artery being 20 mm. of Hg.

The work for both ventricles is 100 grammeters per beat, or 10,111 kilogrammeters in 24 hours. Inasmuch as the heart wall must contract upon a larger volume and is thinner at the beginning of systole than at the end, the amount of work done at the beginning of cardiac contraction is greater than at the end. Therefore, unrestricted diastolic filling of the heart is not an unqualified advantage.

THE PULSE

The Cause of the Pulse Wave—An impulse imparted to an incompressible fluid at one end of a rigid tube is instantly propagated from one molecule to another to the opposite end of the tube. If the tube were filled with compressible gas, as, for instance, air, an appreciable length of time would be occupied in the transmission of the impulse from one end of the tube to the other.

If an impulse is imparted to an incompressible fluid contained in an elastic tube an appreciable length of time is also required for the transmission of the impulse through the length of the tube.

This is true because the force of the impulse transmitted to the fluid is expended equally in all directions and part is spent in the distention of the walls of the tube. That part which is propagated forwards is resisted at first by the column of fluid in front, but finally accelerated by the recoil of the elastic walls of the tube, so producing an exactly similar effect upon a more distal segment of the tube. By this mechanism a wave is transmitted in the fluid from one end of the elastic fluid to the other.

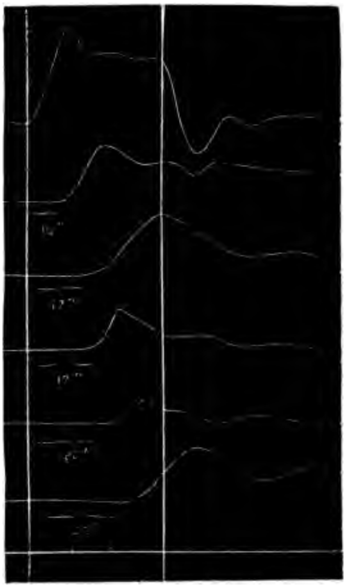


Fig. 37.—Illustrating the Pulse Waves in the Arterial System. (Waller.)

Made by taking simultaneous tracings in the various arteries from above down as follows: 1, The heart; 2, the carotid; 3, the femoral; 4, radial; 5, the anterior tibial; 6, by a plethysmograph on the foot. Time =.1 sec.

The Velocity of the Pulse Wave—The wave of fluid caused in the arteries by the discharge of blood into them at each systole produces a wave in the arterial wall and is called the pulse. It is transmitted with a velocity of 7 meters a second. (Fig. 37.) The velocity of the transmission of a pulse wave is entirely different from the velocity of the flow of the blood. The two must not be confounded.

The Factors upon Which the Velocity Depends—The velocity of the pulse wave depends upon the following factors:

1. The acceleration due to gravity.
2. The elastic coefficient of the wall.
3. The thickness of the wall.
4. The diameter of the tube.
5. The density of the fluid.
6. The propelling force and a constant.

Its Length—The speed of a pulse wave is 7 to 10 meters a second. Its time in passing any one point corresponds to that of one cardiac cycle, namely .8 of a second. Its length would, therefore, be the product of these two numbers, i.e., 5.6 to 8 meters.

Factors Causing a Variation in the Character of the Pulse Wave—We may call the pulse wave above described the main positive wave. Any record of such a wave will be complicated by secondary waves. If, for instance, the end of an elastic tube transmitting a wave is closed at its distal end as soon as the wave reaches the end, it will be reflected back as a reflected wave and be nearer to the main positive pulse wave at points progressively nearer to the distal blocked portion of the tube. If the inrush of fluid into an elastic tube is suddenly stopped a negative secondary wave is started behind the on rushing fluid and travels the whole length of the tube. Similarly if the distal end of the elastic tube is opened the sudden outrush of the propelled fluid will cause a negative reflected wave, which is transmitted backwards through the whole length of the tube. In the human body reflected waves must take place at each division point of an artery, but these points are so multitudinous that all these various waves unquestionably neutralize each other.

Methods for Recording Pulse Waves—Instruments for recording pulse waves are called sphygmographs. As cardiometers for the heart they make their tracings upon a moving surface by a lever or ray of light which is moved by the oscillations of a tambour. (Fig. 38 A and B.)

The Character of a Typical Pulse Wave—A typical pulse tracing presents a rapid upward stroke and a slower downward stroke, the latter containing one main and not infrequently other secondary rises and falls. (Fig. 39.)

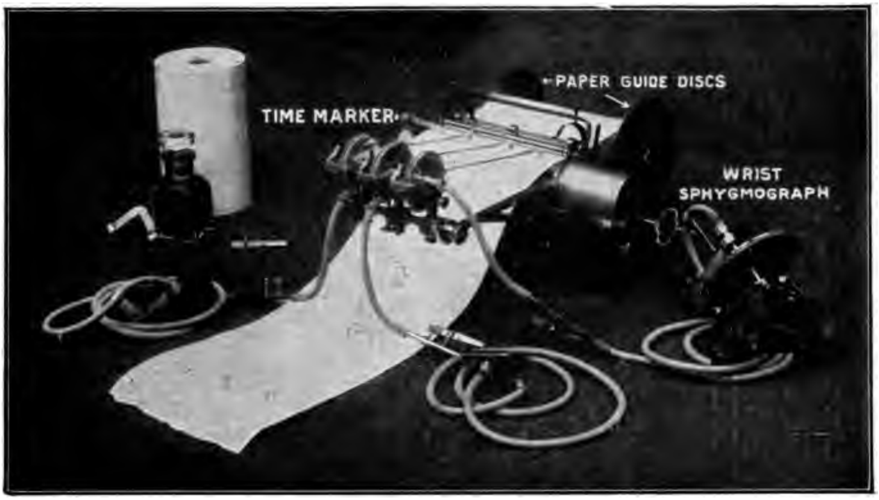


FIG 38A

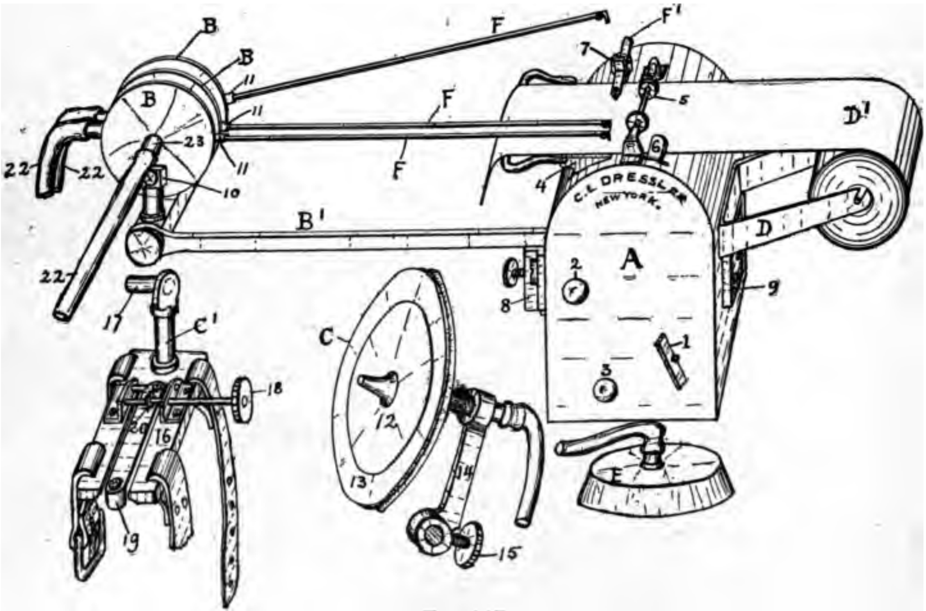


FIG. 38B

FIG. 38, A AND B.—THE MACKENZIE POLYGRAPH.

Upon the paper moved by clockwork are recorded in ink simultaneous tracings of the apex-beat, the radial pulse and the jugular pulse.

The first upward stroke corresponds to the emptying of the blood into the aorta by the systole of the heart. It is called the primary or percussion wave. At varying distances from the summit of this curve are the secondary undulations. The most important one of these is called the dicrotic wave, and the notch preceding the rise of this wave is called the dicrotic notch.

It coincides with the sudden relaxation of the ventricle and the closure of the aortic valves. It is, in other words, a negative wave transmitted peripherally and due to the sudden cessation of the onrush of blood. The dicrotic depression is immediately succeeded by an upward stroke, the dicrotic wave. This is a positive impulse started by the rebound of the fluid against the aortic waves.

Fig. 39.—Normal Pulse-Curve from Radial Artery. (Starling.)

In many pulse tracings two additional secondary waves are recorded, one immediately before and one immediately after the dicrotic notch. The one before the notch is called the predicrotic wave and the one after it the postdicrotic wave.

The predicrotic wave may be regarded as elastic oscillations set up in the arterial systems by the sudden rise of pressure, and the postdicrotic as similar oscillations set up by the dying away of the maximum pressure.

Factors Which Change the Character of a Typical Pulse Tracing—Both these pre- and postdicrotic waves are much increased by the distorting effects due to the fling of the recording mechanism.

The exact position on the pulse curves of these secondary waves, as also the height of the main elevations of a pulse, is much influenced by the strength of the heart beat and the pressure in the arteries. When the first set of secondary waves occur on the ascending curve of the primary pulse wave they are called anacrotic. When they occur entirely on the descending portion they are called catacrotic. (Fig. 40.)

When the peripheral resistance is high, blood will pass into the aorta under conditions of a rising aortic pressure during the whole

of the systole. Secondary oscillations in the pulse will then appear during a period of rise in pressure, i.e., on the upward curve of the pulse tracing, and the pulse will be anacrotic. When, however, the arteries are dilated and the peripheral pressure is low the pressure in the aorta may begin to fall before the systole is finished, the blood running out of the peripheral vessels faster than it is pumped in. Particularly when, as usually happens with a low

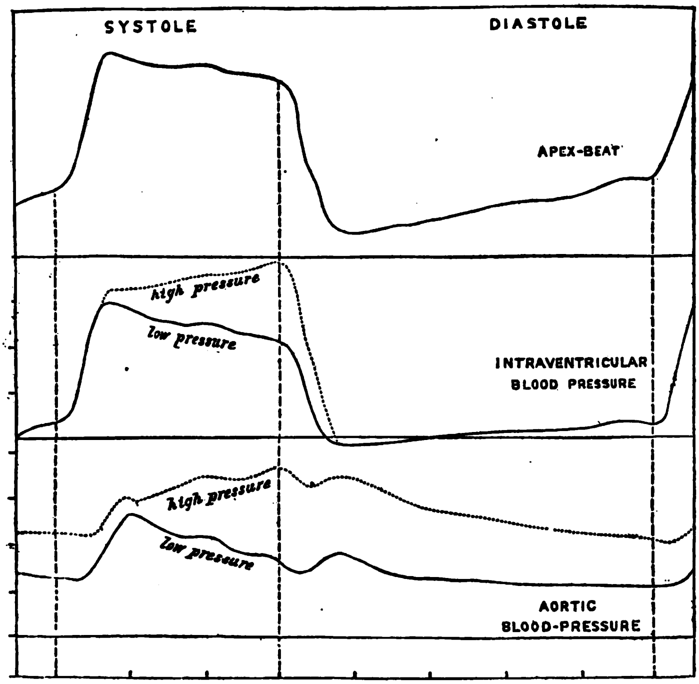


FIG. 40.—DIAGRAM AFTER HURTHLE (CONSTRUCTED FROM DIRECT OBSERVATIONS ON THE DOG) TO ILLUSTRATE SYSTOLIC AND DIASTOLIC PRESSURE-VARIATIONS OF THE VENTRICLE AND AORTA ON MAN.

The noteworthy points of the tracing are: The similarity between apex-beat and intraventricular pressure; the greater postsystolic negative pressure in the ventricle than in the aorta during systole; the unvarying duration of systole at high and at low blood-pressure; maintained pressure in the aorta; the negative pressure (diastolic notch) immediately followed by the diastolic wave. At "low pressure" the systolic pressure in the aorta is double the diastolic pressure; in the high-pressure curve (dotted lines) the difference is proportionally smaller, i.e., a systolic augmentation of ¼ to ⅓ of the mean arterial pressure. Notice that the systolic pressure augments from beginning to end at high pressure, and falls from beginning to end at low pressure. The first tracing is a cardiometer tracing. (Waller.)

peripheral resistance, little blood is thrown at each systole into the aorta. Under these conditions the secondary oscillations will appear on the descending curve of the pulse wave.

No secondary vibrations independent of instrumental deformation occur within the heart during the period of endocardiac rise in pressure; neither is there a true systole plateau to the endocardiac pressure. In the aortic curve of blood pressure secondary oscillations appear at the first falling of the rapid rise of pressure. Then comes the dicrotic wave. Again at the end of the diastole a second set of oscillations appear, which represent the vibrations set up by the beginning of the ventricular contraction.

All these secondary vibrations diminish as the wave progresses to the periphery. Well-marked secondary oscillations in the aorta may be absent in the fermoral artery.

By accurate records of the pulse much information may be gained regarding the character of the circulation. This includes the force and frequency of the heart and strength of the heart beat, its output per beat and the blood pressure in the arteries. Even by feeling the pulse the changes in it which indicate these characters of the circulation may be appreciated.

The Different Varieties of Pulse—A pulse may vary, therefore in

1. Frequency; it may be rapid or slow.
2. Amplitude; it may be large or small.
3. Velocity; it may be characterized by a speedy or slow change of its excursions; it may thus be quick or leisurely.
4. Tension or pressure; it may be hard or soft.
5. Strength; it may be strong or weak.
6. Regularity; it may be regular or irregular.
7. Rhythm; it may be intermittent or regular.

When the peripheral tension is low and the heart strong, as in many fevers of long duration, the dicrotic wave is apt to be particularly well marked. The pulse may then be spoken of as dicrotic. (Figs. 41, 42 and 43.) When the force of the heart is unimpaired, but there is some injury to the aortic valves, allowing some of the blood to leak back into the heart during diastole, there

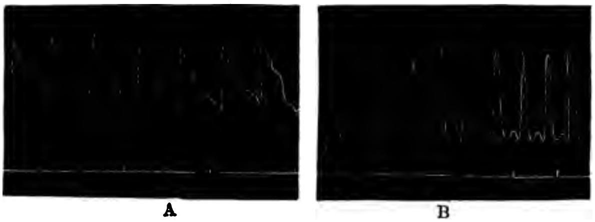


Fig. 41.—Pulse-Tracing Before, A, and After, B, the Inhalation of Nitrite of Amyl.

Tension diminished and frequency increased. The pulse is large and very soft, with fast rise and fall and marked dicrotic wave. (Waller.)

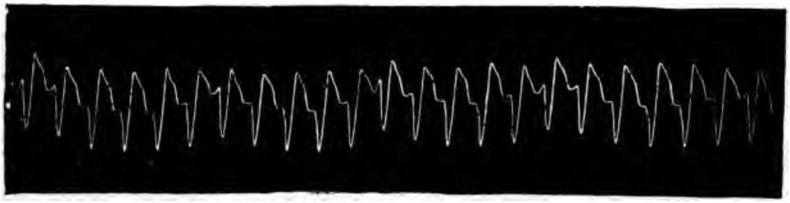


Fig. 42.—Carotid Pulse-Curve During Convalescence After Typhoid Fever.

The pulse is large and soft with well-marked dicrotic wave.

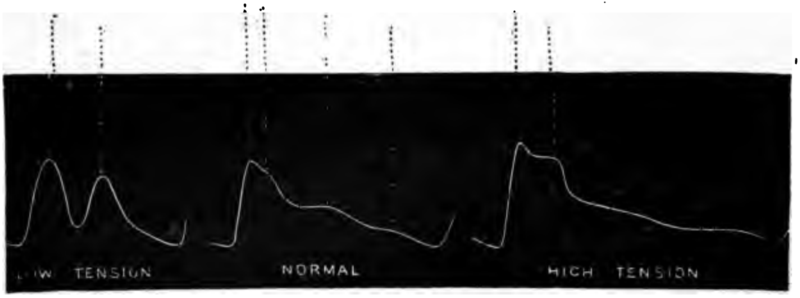


Fig. 43.—Illustrating the Different Character of the Pulse-Wave Under Varying Conditions of Arterial Blood Pressure.

The characteristic features concern the character of the dicrotic wave.

will be a quick rise of pressure and a very rapid fall. Such a pulse is characteristic of the condition of the aortic valves. It is called the water hammer pulse.

PLETHORA AND ANEMIA

The Effect of Increasing the Total Volume of Blood by the Injection of Saline Fluid—The total volume of the blood may be increased by the injection of normal saline solution or of defibrinated blood or of the blood from another individual. When saline solution is used because dilution of the blood occurs the condition is called hydremic plethora.

The increase of the total volume of fluid in this manner does not increase materially the arterial blood pressure unless it has been much diminished as a result of hemorrhage.

Any increase in the arterial pressure is not proportional to the amount of fluid injected. The venous pressure does, however, become greatly increased; all the veins are much distended. More blood is returned to the heart and the cardiac output is increased. The body, however, prevents the rise in arterial blood pressure by relaxing the arterioles. There is a diminution of the difference between the arterial and venous pressures, but, notwithstanding this fact, the velocity of the circulation is increased, even to five or six times, from the injection of an amount of salt solution equal to 50 per cent. of the total volume of the blood.

The work of the heart is also increased, because, notwithstanding the arterial dilatation, there is—

1. Some rise in arterial pressure.
2. A greater frequency of heart beat.
3. An increased cardiac output.

How the Condition Is Relieved—Relief to the plethora is accomplished by—

1. The arterial dilatation.
2. A leakage of the fluid in the form of lymph from the capillaries of the intestines and liver.
3. A copious flow of urine from the glomeruli of the kidneys.

Even within two hours after the injection the total amount of fluid injected may have been eliminated.

How the Reaction from Transfusion Differs—Recovery from excessive degrees of transfusion cannot be accomplished in the same manner.

Compensation During Anemia—The opposite condition to plethora is anemia. When the total volume of blood is diminished the body maintains the arterial pressure as far as possible by three changes:

1. Increased arterial constriction.
2. Increased frequency of heart beat.
3. A transfer of fluid from the tissues into the blood through the thoracic duct.

This transfer is the direct result of the fall in the capillary blood pressure.

The transfer is extremely rapid, occurring even during the course of the bleeding; extreme thirst is a consequence of the loss of the fluid by the tissue, and if gratified will lead to the replacement of fluid to the tissues. The solid constituents of the blood are only slowly replaced.

THE PULMONARY CIRCULATION

The Total Amount of Blood Contained in the Pulmonary Circulation—All the blood in the body must pass through the lungs immediately after making the circuit of the body and before it can start again on that circuit. The lungs, therefore, must be viewed as inserted, as it were, between the vessels of the body and the heart.

The amount of blood which they contain varies much with respiration. At the height of inspiration they contain 1/12 of the whole amount of blood of the body, and at the end of the expiration between 1/15 and 1/18 of the total volume of the blood. In any case, however, there is passing through the combined sectional area of their arterial or venous circulation per unit of time the same amount of blood as is pumped out to and received from the systemic circulation.

The Special Characters of the Pulmonary Circulation—The pulmonary circulation is characterized by a number of peculiarities.

1. The blood pressure in the pulmonary artery does not exceed 15 to 20 mm. of Hg.
2. The arterioles of the lungs have very little muscular tissue and consequently very little power of contraction or control over the amount of blood passing through the lungs.
3. The capillaries of the lungs are wide.
4. Vasomotor nerves coming from the third, fourth and fifth dorsal nerves have been described, but their existence is extremely doubtful and cannot be demonstrated.

Injection of adrenalin produces no contraction of the vessels of the lung. Inasmuch as it specifically causes a contraction of all vasomotor nerve ending, its failure to give evidence of this in the pulmonary circulation indicates the absence of the muscular mechanism for vasoconstriction in the lungs.

Effect of Respiratory Changes in the Pulmonary Circulation and the Effect of the Descent of the Diaphragm upon the General Arterial Pressure—Little obstruction is offered to the passage of blood through the lungs. The arterial blood pressure is affected by respiration. It rises with each inspiration and falls with each expiration; but both these changes in pressure last over into the succeeding phase of respiration. Thus the rise on inspiration lasts into the first portion of expiration. The lungs, therefore, are capable of acting as a passive reservoir for the blood passing from them to the left heart.

The explanation of the rise of general arterial pressure upon inspiration depends upon the flow of a greater quantity of blood into the lungs as a result of the diminished intrathoracic pressure within the thorax during the enlargement of the chest by inspiration. A larger quantity of blood flows, therefore, to the heart and is pumped into the arteries, so that, as an ultimate result, the arterial blood pressure is raised.

The reverse of these conditions accounts for the fall of pressure during expiration. During inspiration another cause operates to hasten the blood to the right side of the heart and hence also to the lungs. This is the descent of the diaphragm; by the contraction of the diaphragm the intra-abdominal pressure is raised and the blood in consequence is pressed from the inferior vena cava toward the

heart; we must consider the pulmonary circulation as passing between two elastic bags. The one bag is the alveoli of the lungs; the other is the thoracic cavity. Within both of these the air pressure during expiration, but more so during inspiration, is less than the normal atmospheric pressure. The two bags tend to pull away from each other and, therefore, to enlarge the capillary space with varying degrees of force.

Still another factor in the relation of respiration to the blood pressure is the varying intrathoracic pressures upon the pericardium. The relative importance of this last factor is open to discussion. Lewis, for instance, regards the varying pressures upon the pericardium during respiration as more important than alterations in the pulmonary capacity. The differences, for instance, which he finds between the effects of deep intercostal and diaphragmatic inspiration appear to him to demonstrate that other conditions are subsidiary. For instance, a deep intercostal inspiration gives a fall of blood pressure, while a deep diaphragmatic inspiration gives a rise of pressure.

Effect of Reflex Influences from the Alveoli—During normal respiration it will be noticed that the heart tends to beat a little more slowly in the downward curve. This difference in rate between inspiration and expiration disappears after division of the vagi nerves. It is, therefore, due to a reflex action passing up to the cardiac center by the vagus nerve from the alveoli of the lungs and down again by the efferent cardiac nerves to the heart.

In contrast to the flow of blood through the pulmonary capillaries the flow through the systemic capillaries is directly controlled by the caliber of the arterioles.

THE SYSTEMIC CIRCULATION

The Appearance of the Flow of Blood through the Systemic Arterioles, Capillaries, and Veins—The flow of blood through the capillaries is best studied by observing it directly with the microscope through some thin membrane, as the web of a frog's foot.

In the small arteries the flow of blood will be rapid and pulsatile. There will be a central zone containing all the corpuscles hurrying rapidly through the vessel. Between the central zone

and the vessel wall will be a clear zone of colorless plasma about .01 of a mm. in diameter.

In the capillaries the flow of blood is inconstant, sometimes almost stopping, and again more rapid. It is always very slow and there is not a peripheral clear zone. As the blood corpuscles come to division points of the capillaries, or for that matter in the arterioles also, they can often be seen to bend or change in shape as they are forced against the dividing place in the vessels. So also as they interfere with each other in passing through the capillaries they change their shape as they are forced by obstructing places.

The varying rapidity of circulation through the capillaries depends upon changes in the caliber of the supplying arterioles. Sometimes only one, never more than two, corpuscles can pass abreast through the capillaries.

The Possibility and Causes of Variations in the Lumen of the Capillaries—The capillary wall consists of only a single layer of endothelial cells, through which diffusion can readily take place. It is a question of much importance and of great interest whether these endothelial cells are endowed with contractile power. If they are, and we believe that they are, they must greatly influence the blood pressure and variations in the distribution of the blood in the body. Changes in the caliber of the capillaries, independent of changes in the arterioles, is a very different matter from passive changes in the capillaries, which depend upon changes in the caliber of the arterioles. It is said that the cells of the capillaries are arranged in strands which pass from the nuclei around the capillary, and in the nictitating membrane of the frog they have been shown to possess a contractile power. If they do contract, they must do so in response largely to chemical stimuli. In any case, it can readily be appreciated how difficult it must be to distinguish a true contraction from a change in caliber due to alterations in the caliber of the arterioles.

Capillary Blood Pressure and Methods of Measuring It—The capillary blood pressure is measured by the weight necessary to obliterate the capillary flow through the superficial layers of the skin or mucous membrane. This pressure may also be applied through a smaller but similar bag to that used for the measurement of venous blood pressure. The obliteration is accomplished when

blanching of the surface has been produced. There are many inaccuracies in this method, and obviously the capillary blood pressure is so closely dependent upon the relation between the pressures in the arterioles and venules that measurements of the variations in the pressures in these afferent and efferent vessels will form a very accurate means of estimating the capillary blood pressure, although it stands in a closer relationship to the pressure in the venules than in the arterioles.

If both a rise and fall of the arterial and venous pressure, the capillary pressure must rise or fall with them. When one rises and the other falls it may be difficult to say what happens to the capillary pressure.

Factors Originating in the Capillaries Themselves Which Influence the Capillary Blood Pressure—The resistance to the flow of blood through the capillaries depends upon the internal friction of the capillary walls and the viscosity of the blood. These factors will cause a diminution of the capillary blood pressure as it flows from one end of the capillaries to the other end.

It has been estimated that the diminution of the capillary blood pressure at the end of a capillary from that at its beginning never amounts to more than 150 mm. of blood or 10 mm. of Hg. It usually is one-eighth to one-half of this amount.

The Different Capillary Pressures—In the horizontal position the capillary blood pressure is about 10 mm. of Hg. It is influenced by hydrostatic pressure. At the end of the finger it varies as follows with the distance of the finger below the head:

0 mm. below the head equals 328 mm. of water.
205 mm. below the head equals 329 mm. of water.
490 mm. below the head equals 513 mm. of water.
840 mm. below the head equals 738 mm. of water.

The Factors Influencing the Return of Blood through the Veins—The mechanism of the flow of blood through the veins is quite as important as that through any other portion of the vascular system. Upon the quantity of blood passing back to the heart through the veins depends absolutely the maintenance of any circulation at all. The blood meets with only a negligible resistance aside from hydrostatic pressure in its passage through the veins back to the heart. Its passage back to the heart will depend solely

upon a progressive diminution of pressure in the direction from the periphery of the body toward the heart.

The pressure in the great veins near the heart is below 0 most of the time. During each inspiration this minus pressure is increasing, so that during inspiration blood is sucked toward the heart. During diastole the heart yields to the negative pressure in the chest and takes regularly a definite quantity of blood from the great veins. This amount must in turn be made up by the flowing of more blood into the great veins from the periphery.

This explanation meets perhaps all the factors of the problem when the body is in a horizontal position. What, however, explains the return of blood from the lower limbs in the upright position of the body? We would naturally expect that this position would greatly increase the pressure of the blood in the venules of the foot by an amount equal to the difference between level of the foot and the heart.

As a matter of fact it does not. It is true that the blood pressure in the veins of the foot in the upright position of the body is higher than that of the veins of the hand when the latter occupied the level of the heart.

Indeed, if we should subtract the hydrostatic pressure measured in terms of blood and representing the distance between the level of the foot and heart from the actual pressure in the veins of the foot, we would have a minus pressure of 40 cm. of blood. Hill has stated that there is very little difference between the blood pressure in the capillaries of the hand and those of the foot, and has shown that when a man assumes the upright position the arteries of the leg contract, thus holding back the blood from the leg and so completely controlling the amount of blood entering the capillaries that the intracapillary blood pressure is not raised proportionally to the degree with which the foot is depressed below the heart when the upright position is assumed.

Of course, any increase of hydrostatic pressure in the venules will be equaled by an increase of hydrostatic pressure on the arterial side, so that in the presence of unyielding walls in the veins and arterioles the progressive difference in pressure between the aorta and vena cava, due to the propulsive force of the heart, will still be effective in returning the blood through the veins.

The unyielding walls upon the arterial side of the circulation

are furnished by the contracting arterioles, and upon the venous side of the circulation support is furnished to the veins by the normal tone of the skeletal muscles and the increased pressure which they exert during voluntary contraction and the pressure of fascial planes.

Variations of the capillary blood pressure as the hand occupies different levels indicate that equalization by hydrostatic pressure on the two sides of the capillaries plays a part in the return of the venous blood to the heart. The low blood pressures found in the venules of the foot, however, indicates that the most important factor in the return of venous blood certainly in the lower extremity is the contraction of the vouuntary muscles and the support of fascial planes. These contractions compress the veins and so force the blood on toward the heart. Their efficiency is maintained by the presence of little valves in the veins which prevent any flow backwards toward the capillaries. Each segment of a vein between two of these valves compressed by the muscles external to the vein may be considered as an additional heart propelling the blood on to the main pump of the body.

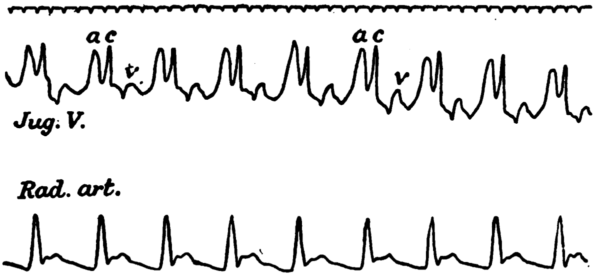


FIG. 44.—VENOUS PULSE-TRACING FROM JUGULAR VEIN COMPARED WITH THE ARTERIAL PULSE-TRACING FROM THE RADIAL ARTERY. (Starling.)

Venous Pulse Tracings—Tracings taken from the jugular veins show definite changes of pressure within the veins which correspond to changes in the intra-auricular pressures. There are three definite pulsations of the veins with each cardiac cycle, and each of these produces a wave in the tracing. (Fig. 44.)

There is a large wave due to contraction of the auricle followed almost immediately before the fall of the first wave is complete by *a wave of* equal height due to the increase in auricular pressure

caused by the contraction of the ventricle. The curve then falls to the base line and rises again a short distance to produce the third wave as the auricle fills with blood.

THE PHYSIOLOGY OF THE HEART

The Great Functional Characteristic of Heart Muscle—Functionally the heart muscle presents differences from other muscle tissue which, even though they may be explained entirely as differences in the degree with which muscle manifests its activity, are nevertheless so striking that they indicate a special differentiation in function. The first striking characteristic of heart muscle is its automaticity. An excised heart of a cold-blooded animal, as a frog or tortoise, will continue to beat with a normal sequence of the various chambers for hours or days, provided it is kept cool and moist. The heart of a warm-blooded animal will also continue its activity under proper conditions for surprisingly long periods. Thus the heart contains within itself a complete mechanism for its own activity, and, cut off from all connections with the central nervous system, it is able to maintain its own rhythmic contractions.

The Nervous Tissue of the Heart—Though cut off from all nervous connections, the heart is not devoid of nervous tissue. A collection of ganglia cells, the ganglion of Remak, exists in the sinus venosus. Another collection exists near the auriculo-ventricular grove (Bidder's ganglion). From these collections of nerve cells fine non-medullated fibers pass to all parts of the heart wall.

The Possible Relation of the Nervous Tissue of the Heart to Its Automaticity—It is very natural to assume that the cause for the automaticity of the heart's action resides in these ganglia, in other words, that the heart is capable of a spontaneous rhythmic pulsation because of impulses which are started by the nerve cells in these ganglia. A number of facts lend color to this view.

The Effects upon the Heart's Automaticity of Applying the Stannius Ligature Progressively Nearer the Apex of the Heart—If the sinus of the frog's heart is separated from the rest of the heart by cutting the heart across between the sinus and the auricle or by applying a ligature around the sino-auricular juncture (Stan-

nius ligature), the sinus will go on beating with its own rhythm, but the ventricle and auricle will stop beating altogether for a time. After the lapse of five minutes to half an hour the auricles and ventricles will begin again to beat, at first slowly and a little later more rapidly, but never as rapidly as the rhythm of the sinus. If now instead of dividing the heart at the sino-auricular juncture the section is placed at the auriculo-ventricular juncture, the sinus and auricles will go on beating with their normal rhythm, but the isolated ventricles will only begin to beat again slowly and after the lapse of a much longer time than is the case with the auriculo-ventricular preparation. If a third preparation is made consisting only of an apex of the heart, the isolated portion will not beat again at all. It may respond by a single contraction to one induction or galvanic shock, but it cannot spontaneously start beating again or be stimulated by ordinary means to maintain continued rhythmic contraction.

We see, therefore, that there is a progressive diminution of the power to originate and maintain rhythmic contractions in the isolated lower third of the frog's or tortoise's ventricle. Supplied with salt solution by perfusion under pressure or by the passage of a constant current or continued weak induction shocks, it will begin to rhythmically contract.

The above facts in reality lend no support to the theory of the nervous or ganglionic origin of the automatic rhythmic activity of the heart, they do not contradict the myogenetic theory of the origin of the cardiac contractions, while the following facts demonstrate that the heart muscle itself is alone responsible for the automaticity of its activity.

By crushing above the apex of the heart the latter can be separated from the rest of the heart by a cone of crushed and functionless tissue, but the apex will still remain attached to the heart, so that the heart will not leak. Only the portion of this heart above the crushed zone will contract automatically. If, however, the intraventricular pressure is raised by clamping the aorta, the apex will once more contract rhythmically.

It is possible to cut out a strip of muscle free from any ganglion cells from the apex of the tortoise heart; such a strip will enter into rhythmic contractions under the stimulus of salt solution in a moist chamber.

In the frog's heart and still more easily in the tortoise heart it is possible to excise nearly all the ganglia and nerve fibers of the heart without interfering with the rhythmic contractions of the heart. (Fig. 45.)

The chick's heart beats before ganglion cells and nerve fibers have been developed within it.

Remak's ganglia are developed in connection with the vagus nerve and where this nerve enters the heart. The cells of the ganglion mark the transition between the post and preganglionic fibers of this nerve. Nicotin possesses a selective paralyzing action on ganglionic cells. After its application to the ganglia stimulation of only the postganglionic fibers of the vagus nerve will produce slowing of the heart, a fact which demonstrates that after the painting with nicotin the ganglionic cells are functionless.

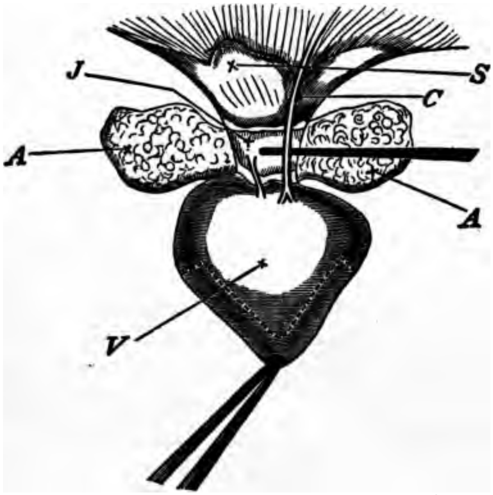


FIG. 45.—VENTRICLE OF THE TORTOISE HEART TURNED OVER, TO SHOW THE CONNECTION OF THE SINUS (S) BY MEANS OF THE JUNCTION WALL (J) WITH THE VENTRICLE (V) AND THE AURICLES (A). THE POINT OF THE SEEKER IS PLACED UNDER THE FREE CORONARY VEIN AND NERVE (C).

The dotted line shows how a strip may be cut from the ventricle without containing nerve tissue. (W. H. Gaskell.)

Under these conditions, that is, after the application of nicotin, the automatic rhythm of the heart is in no way interfered with. The ganglia must, therefore, be regarded as distributing centers for the vagus nerve.

A weak tetanizing current causes local inhibition of the heart's action. Inasmuch as the application of atropin abolishes this effect, these weak currents must act on the finer postganglionic fibers throughout the heart.

The function of these fibers must, therefore, be inhibitory in their nature and not connected with the maintenance of the automatic rhythmic contractions of the heart.

The True Character of the Functional Relation between the Auricles and Ventricles—Normally each cardiac cycle starts at the sinus venosus and proceeds from this structure over the whole heart. The normal sequence is sinus venosus, auricles, ventricles and bulbus arteriosus. After separating these portions of the heart by section or crushing, the rhythm characteristic of each separate portion can be recorded. From the sinus down there is a decreasing rapidity of rhythm. The normal rhythm of the ventricle, that is, that which in the intact heart corresponds with the rhythm of the sinus, depends upon the propagation of an excitation from the sinus to the ventricles.

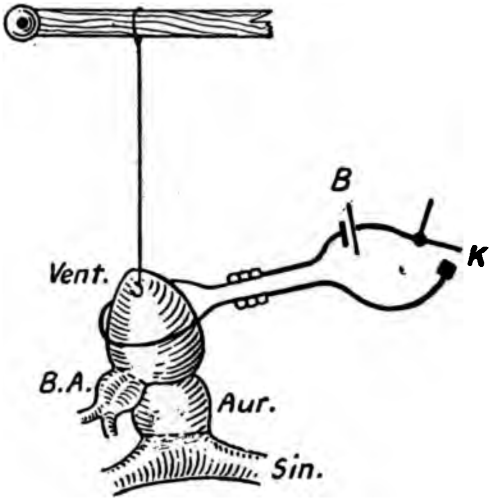


FIG. 46.—ARRANGEMENT OF PLATINUM LOOP THROUGH WHICH A CURRENT CAPABLE OF WARMING THE LOOP MAY BE SENT AND BY WHICH THE HEART MAY BE STIMULATED AT DIFFERENT LEVELS BETWEEN THE APEX AND AURICLES.

The ventricle cannot, in other words, beat with its own rhythm

because it receives from the sinus a stimulus at each beat of the latter which is responsible for its faster rate in the intact heart. The importance of the transmission of impulses through the heart is further emphasized by the fact that it is possible to create a reversed rhythm from ventricle to auricle by stimulating the former at a faster rate than that of the sinus venosus.

The differences in automaticity between the sinus and ventricle are further illustrated by the effect of warming each by a conducting platinum loop. (Fig. 46.) Warming the ventricle will call forth a strong beat without altering the rhythm. Warming the sinus will quicken the rhythm without increasing the force of the beat. The ventricular cell is a more highly differentiated one than the cell of the sinus venosus. In consequence it is more dependent for the manifestation of its activity upon stimulation and its response is a more powerful one. "It is a good servant of the sinus."

The Tissue Transmitting Impulses from the Auricle to Ventricle—What is the tissue which propagates the impulse from the sinus to the ventricle? We have already discussed the impossibility of its being the nerves in the heart.

Moreover, the mere possibility of exciting a reversed rhythm of contractions in a heart is evidence against the view that the nerves of the heart propagate the stimulus resulting in coordinated rhythmic contractions of the whole heart. They could not be the transmitting agent without furnishing an exception to the law of forward direction. The auricle may be slit up by a series of interdigitating cuts in a manner to divide the normal course of any nerve tracts. Still the impulse to contraction will pass around all the cuts from the sinus venosus and finally reach the ventricle, which it stimulates. When the bridges of muscular connections are made exceedingly narrow the wave of contraction halts in a definite pause in its passage over such an auricular bridge. (Fig. 47.)

By soaking the auricles for some time in distilled water they will become incapable of contracting, but still capable of transmitting an impulse. The most obvious explanation of all these experiments is that the muscular tissue of the heart not only originates its own rhythm but serves as the agent by which a uniform rhythm or impulse to contraction is transmitted over the whole heart.

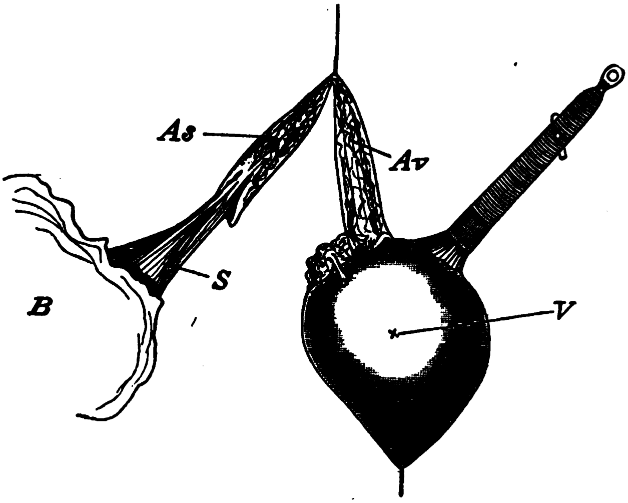


Fig. 47.—Heart of a Tortoise with Auricle Slit Up so as to Separate Auricle into Two Parts, As, Av.

Connected by only a small strand of muscular tissue. (W. H. Gaskell.)

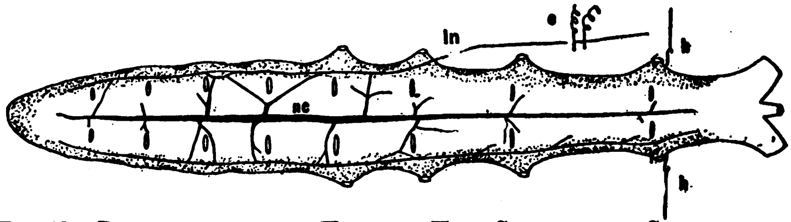


Fig. 48.—Preparation of the Heart of King Crab for the Study of the Local Cardioreflex Dorsal View.

nc, Nerve cord; *ln*, lateral nerves; *h*, hooks for connecting a region of the heart with the lever; *e*, electrodes. The nerve, *in*, may be dissected out for half of its length and used to convey a stimulus to the portion of the heart to which it is still connected.

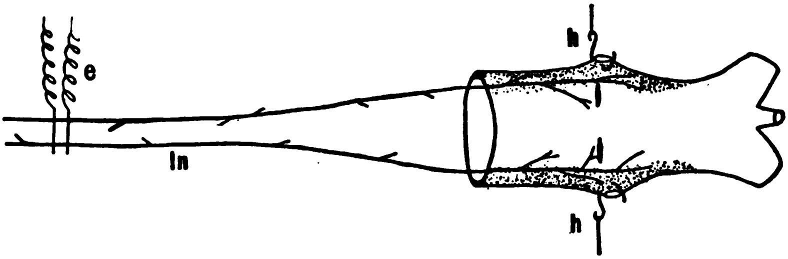


Fig. 49.—The True Muscle Nerve Preparation Which May Be Made from the Heart of the King Crab.

In one of the lower animals, notably the king crab, there seems to be a possible exception to this view, and a large share in the transmitting mechanism is taken by the nerves. In fact, it is possible in the king crab to make a true muscle-nerve preparation of the heart and to stop all transmission by excision of parts of the gangliated cord. This animal, however, must form a special case. (Fig. 48 and 49.)

Time of the Contraction of Heart Muscle—Heart muscle possesses its own time of contraction, while voluntary muscle contracts in about one-tenth of a second. The contraction of the tortoise heart lasts 2 seconds. The contraction of the mammal's heart lasts from .3 to .4 of a second.

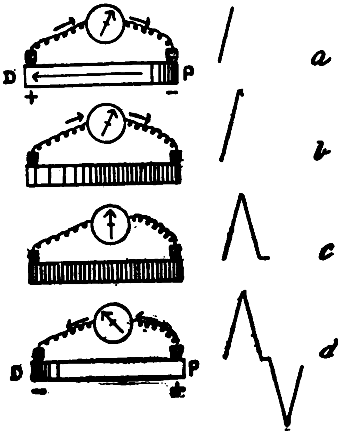


FIG. 50.—DIAGRAM ILLUSTRATING THE DEVELOPMENT AND SUBSIDENCE OF ACTIVITY (AND NEGATIVITY) IN A SINGLE MUSCLE STRIP. RESPONDING TO A STIMULUS APPLIED AT P.

The corresponding and successive phases of the galvanometric curve are shown in the four lines *a, b, c* and *d.* (From Lewis, "Lectures on the Heart," Hoeber, New York.)

The Electrical Changes Which Accompany Cardiac Contraction, the Information Which They Supply upon the Development of the Shape of the Mammalian Heart and the Propagation of the Impulse Controlling Contraction Through the Heart—*The Portions of the Primitive Heart Which Are Represented by the Various Portions of the Mammalian Heart*—A wave of contraction passing over an excised strip of heart muscle is accompanied by a typical *diphasic electrical* change. Any spot passed by the wave becomes

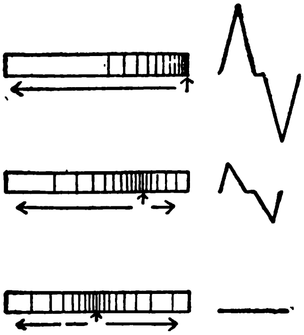


Fig. 51.—Diagram to Show That Maximal Excursion of the Galvanometric Recorder Is Obtained When the Interval of Delay Between the Arrival of the Excitation Wave at the Contact Is Greatest. (From Lewis, "Lectures on the Heart," Hoeber, New York.)

at first negative to all other portions of the muscle and actively positive again as the wave passes beyond the spot. (Figs. 50, 51 and 52.)

The electrical change accompanying the wave of contraction which passes over the intact heart is somewhat more complicated. This is due to the fact that the heart of the frog or mammal has undergone a change from the simple tubular heart of the fish.

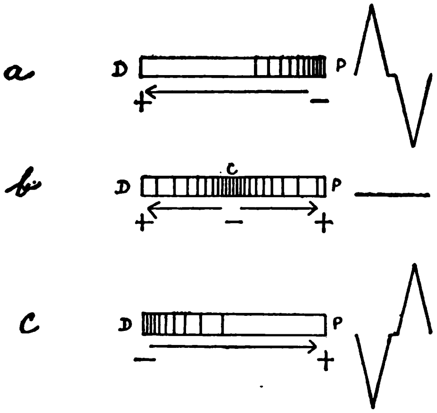


Fig. 52.—Diagram Illustrating the Inversion of the Curve When the Order of Contraction Is Reversed, and Its Isopotentiality When the Ends of the Strip Are Activated Simultaneously.

The directions in which contraction is driven are indicated by the arrows. *(From* Lewis, "Lectures on the Heart," Hoeber, New York.)

In virtue of this change the bulbus arteriosus has rotated from one end of the simple tubular heart to a position at the base of the heart.

There passes, therefore, over the base of the heart of the frog or mammal two diphasic changes. The base is first negative, then positive, as the apex becomes negative, and finally the base becomes negative as the bulbus arteriosus becomes in its turn excited. (Fig. 53.)

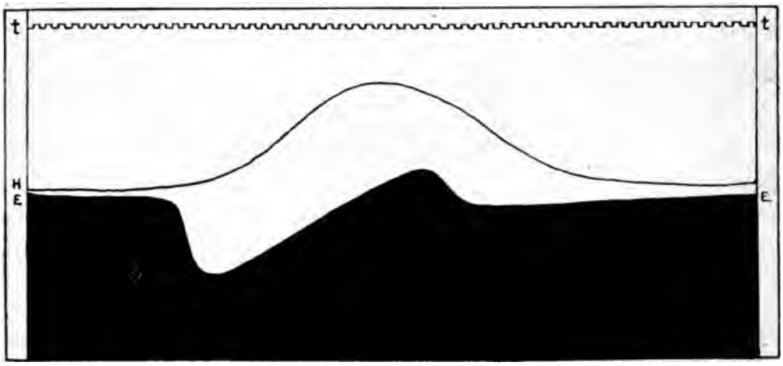


Fig. 53.—A Cardiogram Illustrating a Single Diphasic Change Due to a Spontaneous Contraction of a Portion of a Frog's Heart Muscle.

H is the diphasic electrical change in the heart muscle; E is the simultaneously recorded mechanical change.

Like the frog's heart, the mammal's heart contains ganglion cells around the openings of the great veins, along the borders of the interauricular septum and in the auriculo-ventricular groove.

The Difference in Automatic Power of Contraction Possessed by the Mammalian Heart as Contrasted with That of the Amphibian Heart—The ventricle of the mammal possesses a greater power of automatic rhythmic activity than the ventricle of the frog or tortoise heart. The whole heart of the mammal may be kept beating for hours if it is perfused through its coronary arteries by Ringer's solution or by defibrinated blood. The ventricle of the mammal's heart which has been separated from the auricles, except for fibrous connections, by crushing all nervous and muscular tissue in a plane between the auricle and ventricle, will not stop even for a moment its rhythmic contraction. These

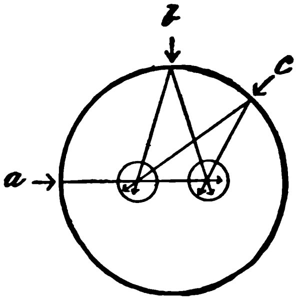


Fig. 54.—Diagram Illustrating Stimulation of a Sheet of Muscle.

The circle represents a sheet of muscle, excited at *a*, *b* or *c*, and examined at two central contact points. The excursion of the recorder is greatest when the contacts are in the line with the point of excitation; i.e., when the muscle is stimulated at *a*. It is least when stimulation is at *b*, for in this circumstance activity is simultaneously developed at the contacts. (From Lewis, ''Lectures on the Heart,'' Hoeber, New York.)

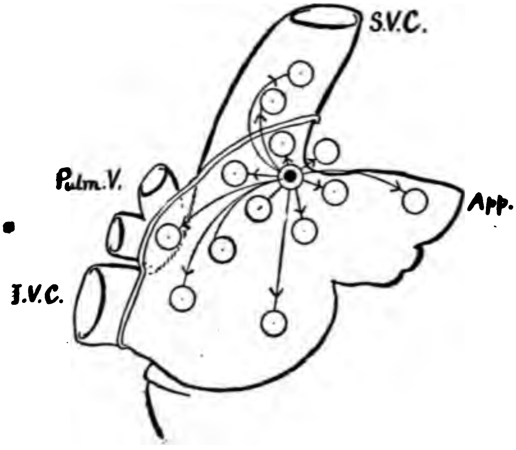


Fig. 55.—The Contacts as Applied to an Auricle.

When the central contact overlies the sino-auricular node, it is invariably relatively negative to outlying points and the height of the curve, which is always proportional to the distance which this state of negativity must travel in order to reach the second contact, can be used to map out the direction taken by the spread of this wave of negativity or the mechanical change which it accompanies over the heart. (From Lewis, ''Lectures on the Heart,'' Hoeber, New York.)

independent contractions of the isolated mammal's ventricles are, however, slower than those of the intact heart.

The Character of the Electrocardiogram Waves in the Human Heart—It is possible to use the electrical variations of the differences in potential between the base and apex of the mammal's heart as an index of the course and time relations of the excitatory wave which passes over a heart. (Figs. 54 to 61.) These may be recorded by leading off a point over the apex of the heart and another point over the right shoulder or right arm in the intact body. (Figs. 62 and 63.)

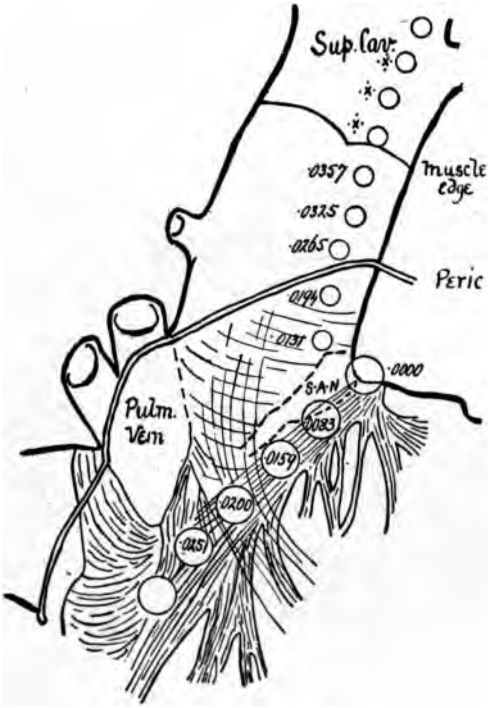


FIG. 56.—SERIAL LEADS OVER THE AURICLE FROM THE SULCUS AND SUPERIOR CAVA.

The times at which the excitation wave appeared at the several contact points are given and make possible the mapping out of the course taken by the excitatory wave. From the highest S.V.C. (contacts marked *) no intrinsic deflections were obtained. (From Lewis, "Lectures on the Heart," Hoeber, New York.)

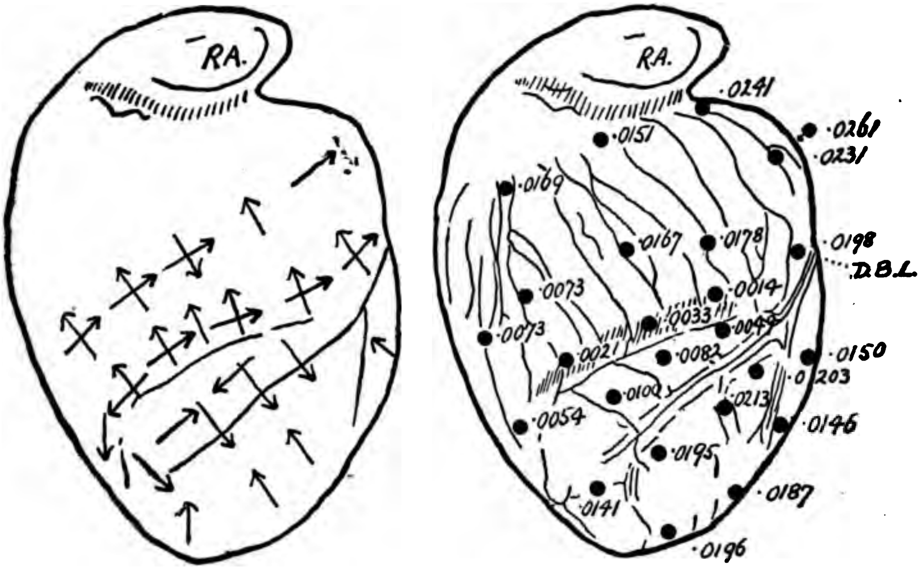


Fig. 57 Fig. 58

FIGS. 57 AND 58.—ILLUSTRATING MANNER IN WHICH THE COURSE OF THE EXCITATORY WAVE MAY BE MAPPED OUT FOR THE WHOLE HEART.

Outlines of the front of the heart in an actual experiment.

Upon Fig. 57 arrows have been drawn; they depict the direction of spread on the front of this heart, investigated by means of closely paired contacts. Here the direction of the deflection was the index.

FIG. 58.—The times at which the excitation wave appeared on the front of the same heart, related to the upstroke of R in the lead II.

R.A., Rt. appendix.

R.B.L., Descending branch of left coronary artery. (From Lewis, "Lectures on the Heart," Hoeber, New York.)

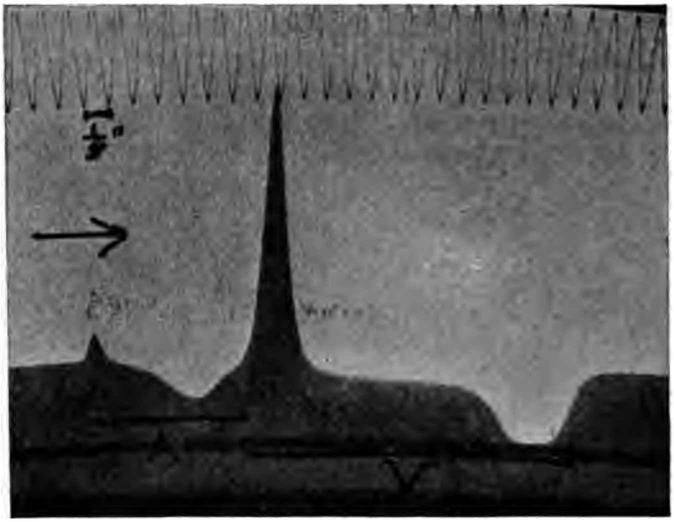


Fig. 59.—Electrometer Record with the Contacts upon the Sinus and the Ventricle Apex Respectively.

Upward movement signifies relative negativity of the sinus contact (tortoise heart). One beat only is shown in the record. (Gotch.)

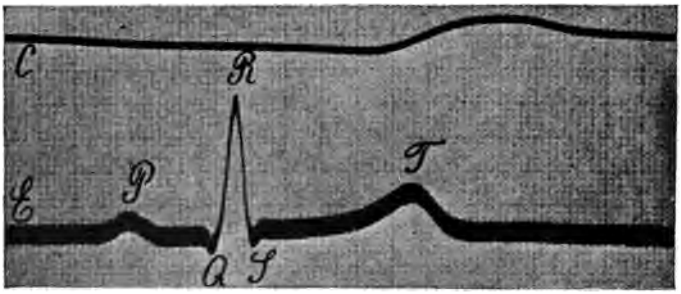
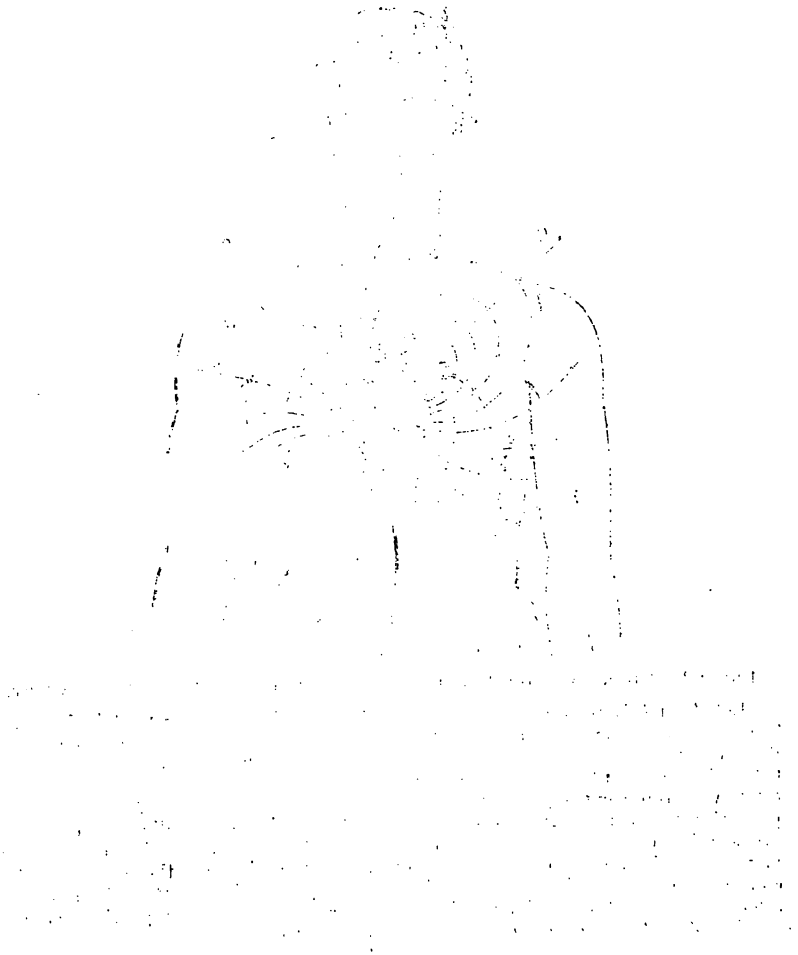


Fig. 60.—Electrocardiogram of Man, Obtained by Leading Off From the Two Hands to a Strong Galvanometer, Taken Simultaneously with a Carotid Pulse Tracing.

C is the carotid pulse tracing. The different parts of the curve are designated by the letters P, Q, R, S, T, first applied to them by Einthoven. (Starling.)



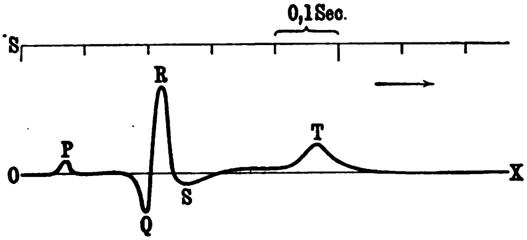


FIG. 61.—SCHEME OF ELECTROCARDIOGRAM.

The P wave represents contraction of the auricle; Q to T represents the total period of ventricular contraction.

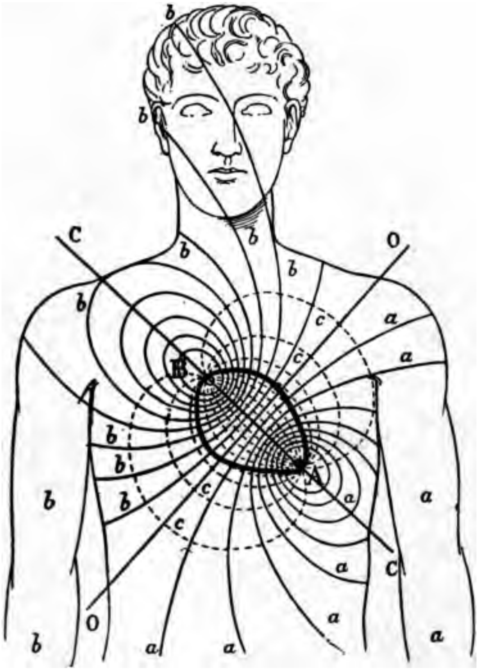


FIG. 62.—CHARACTER OF ELECTROCARDIOGRAM WAVES IN HUMAN HEART.

Let A and B respectively represent apex and base of the ventricular mass. Then, if at any moment a difference of potential should arise between A and B a current, *c c c*, will be established along and around the axis C C; the line O O will represent the plane of zero potential or equator; the lines ***a a a***, ***b b b*** will represent equipotential curves around A and B. A difference of potential between A and B will be manifested if two leading-off electrodes are applied on opposite sides of the equator, O O; no such difference will be manifested if both electrodes are on the same side of the equator. The equator O O will divide the body into two asymmetrical parts, (1) a portion *b b b including* the head and right upper extremity, (2) a portion ***a a a*** *including the three other* extremities. (Waller.)

The waves of such electrical changes recorded on a moving sensitive surface present three typical diphasic variations precisely as if the leading off points were taken from the heart itself.

In fact, the two terminals of the galvanometer circuit may be held in the hands of the patient whose heart's action is being recorded. A typical electrocardiogram shows three waves, each consisting of a rapid rise and fall, in other words, of diphasic variations. The first wave is a small one and is certainly due to the auricular contraction. The high elevation the contraction of the ventricle at the base. The fall of this high wave is due to the passage over the rest of the ventricle of the wave of contraction as the apex becomes negative. The third elevation is a small one and due to the contraction of the bulbus arteriosus in the region of the base. It becomes first negative and then positive as the wave of contraction passes over it.

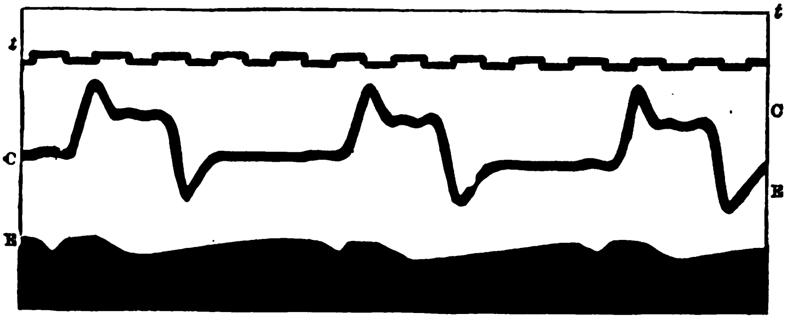


FIG. 63.—CHARACTER OF ELECTROCARDIOGRAM WAVES IN HEART.

Diphasic variation, E E; land simultaneous cardiogram, C C.
The leads-off to the capillary electrometer were from the mouth to the sulphuric acid, and from the left foot to the mercury. Time, *t t*, marked in one-tenth second. (Waller.)

Embryological Units of the Human Heart—The portions of the heart showing these separate electrical variations represent the separate components of the primitive heart, namely, the sinus venosus, auricle, the ventricle and the bulbus arteriosus.

The excitation of the reverse of the sequence of events in the mammal's heart, i.e., a contraction first of the ventricle and last of the auricles, is possible in the human heart by stimulating the ventricle at a rate slightly faster than the normal rhythm of the

auricles. It indicates that the propagation of the impulse over the mammal's heart is not accomplished by the nerves in the heart.

The Bundle of His and Its Transmitting Function—Except for the bundle of His, first described by Kent, there is no continuity of muscular structure between the auricles and the ventricles. This bundle in the human heart begins in the cardiac tissue in close connection with juncture of the superior vena cava and the right auricle (the so-called sino-auricular node). The sino-auricular node consists of muscular tissue of a still more primitive character than the fibers of the bundle of His. It lies in the wall of the sinus venosus between the auricular appendix and the superior vena cava but close to the latter in the groove between it and the right auricle and the superior vena cava. Another node, the auriculo-ventricular node, to be regarded probably as the extension of the

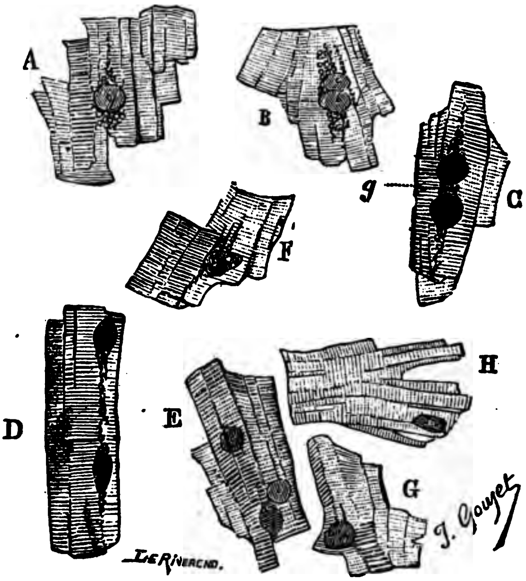


FIG. 64.—ORDINARY MUSCULAR CELLS OF THE HUMAN MYOCARDIUM, SHOWING THE BRANCHING.

The cells have been isolated by teasing a piece of muscle in ammonia picrocarminate.

A, B, C, D, E, F, G, H, muscular cells of the heart of various forms; *g*, granules or striations. (Renaut.)

sino-auricular node, lies at the base of the auricular septum on the right side, below and to the right of the opening of the coronary sinus. It is to be regarded as the first portion of the bundle of His

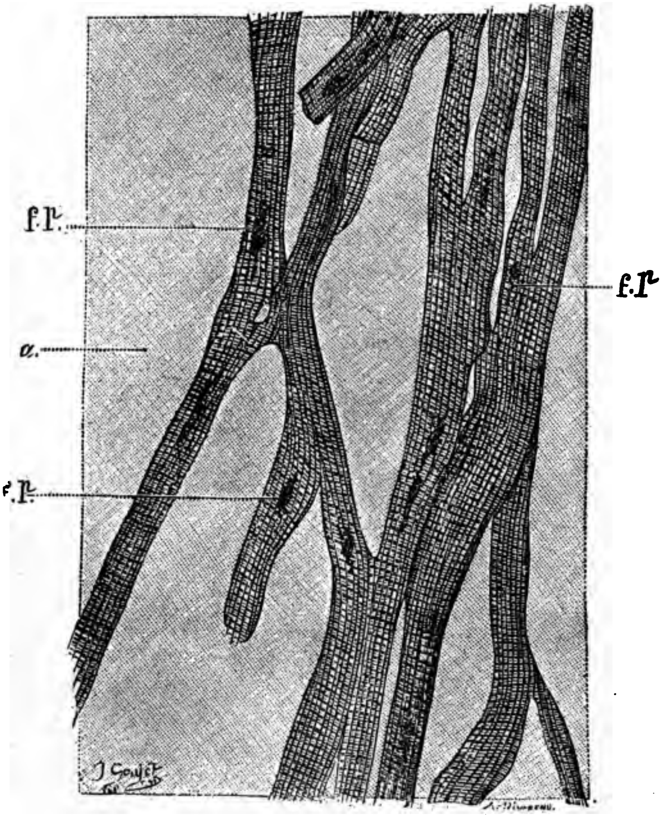


FIG. 65.—ORDINARY MUSCULAR BUNDLES FROM THE HUMAN HEART, FORMING A NETWORK BENEATH THE ENDOCARDIUM, FIXED IN OSMIC ACID.

fp, Protoplasm bulged out by the nucleus of each cell. (J. Renaut.)

which may be said to be intimately associated with the sino-auricular node from which it begins.

Passing along the top of the interventricular septum, the bundle divides into two parts for each ventricle. These two portions pass in the surface of each side of the interventricular septum and into the papillary muscles of each side. From the papillary muscles fiber bands radiate to the apex.

a certain strength to evoke a single contraction. The resulting contraction is, however, always a maximum contraction. There is either evoked a maximum contraction or none at all. The same fact is true for each individual fiber of voluntary muscle, but inasmuch as certain weaker stimuli, when applied to voluntary muscles, will not stimulate all fibers, it is possible to evoke contractions of graded strength in voluntary muscle. The branched and anastomosing character of heart muscle makes possible the transmission of an impulse started in one muscle fiber to the other fibers, so that the heart as a whole will give a maximum contraction or none at all as the result of stimulation.

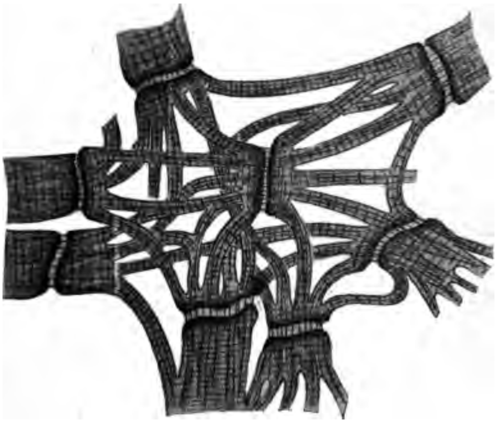


FIG. 67.—A PREPARATION OF THE PURKINJE FIBERS OF THE BUNDLE OF HIS.

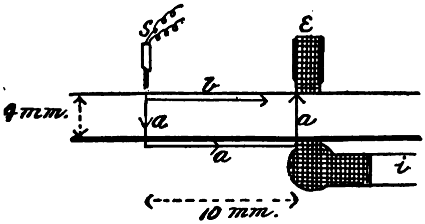


FIG. 68.—Two contacts (*e* = external, *i* = internal) are placed on the epicardium and endocardium respectively, and the heart wall is stimulated at S, 10 mm. away. The excitation appears at a natural interval before it appears at the external contact; it travels therefore more quickly by way of the Purkinje substance. (From Lewis, "Lectures on the Heart," Hoeber, New York.)

tory period of the ventricle following the extra contraction which has been evoked. (Fig. 69.)

Often the ventricular contraction, following the long pause and

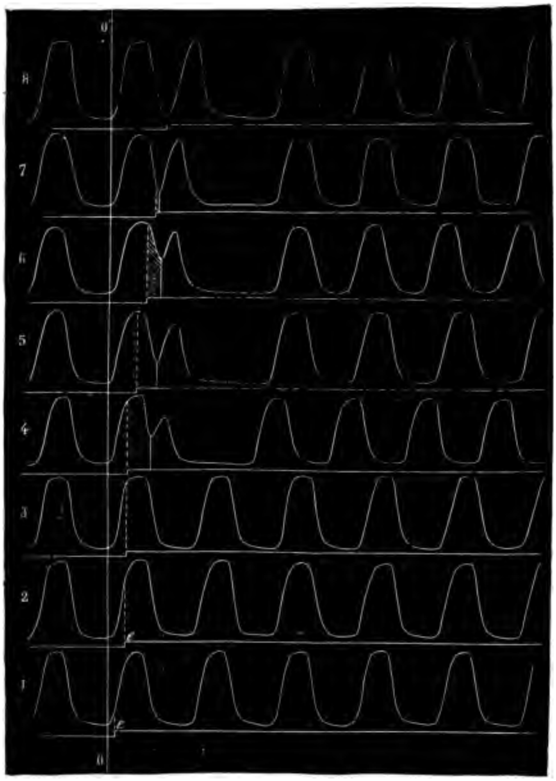


FIG. 69.—TRACING OF SPONTANEOUS CONTRACTION OF FROG'S VENTRICLE TO SHOW REFRACTORY PERIOD.

In each series the surface of the ventricle was stimulated by an induction shock at E, as indicated by the base line of each series. In 1, 2 and 3 this stimulus had no effect since it fell during the refractory period. In 4, 5, 6, 7, the effect of the shock was to interpolate an extra contraction in the series, the latent period (shaded portion) gradually diminishing from 4 to 7 (diastolic rise of irritability). In 8 the irritability was already considerable and the latent period inappreciable.

The compensatory pause after the extra beat is also well shown in 4, 5, 6, 7, 8. (Marey.)

resulting from the second impulse from the sinus venosus, is greater. On account of the refractory period it is impossible to tetanize heart muscle. By using very strong stimuli, as has been indicated,

extra contractions may be intercalated. so that contractions may follow each other rapidly and produce a notched elevated curve somewhat resembling the curve of a tetanus, but differing from a true tetanus in that the summits of the curves representing the extent of the contractions are no higher than single contractions.

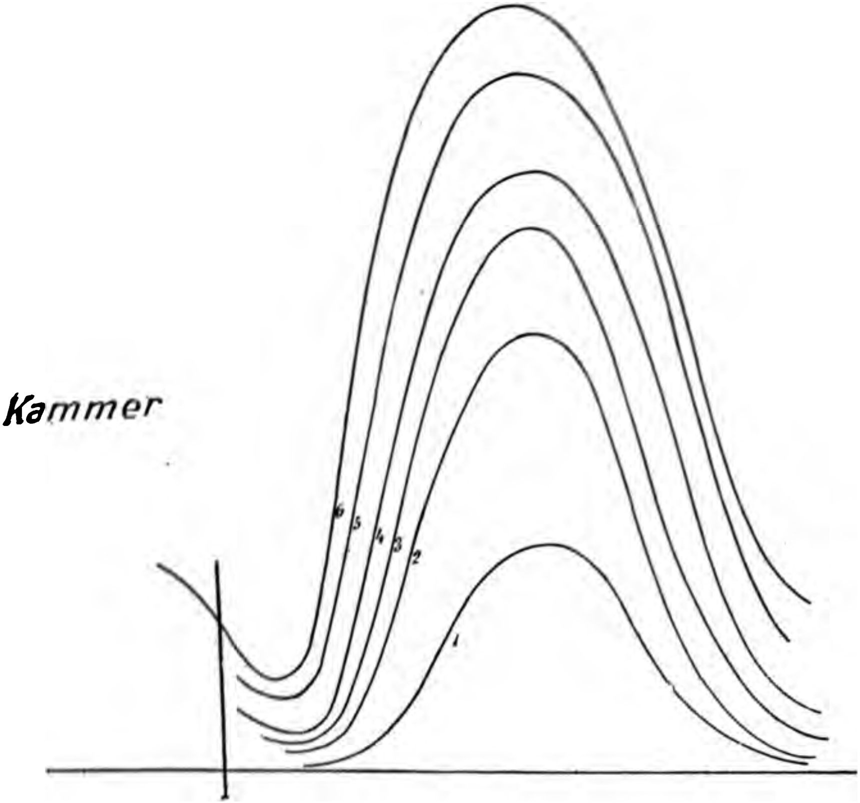


FIG. 70.—CURVES ILLUSTRATING THE PROGRESSIVELY GREATER ISOMETRIC CONTRACTIONS OF HEART MUSCLE DEVELOPED BY INCREASING THE DEGREE OF FILLING OF THE VENTRICLE DURING DIASTOLE.

It must be remembered that no isometric contraction of muscle is absolutely isometric, but only nearly so, and may therefore be measured by greatly magnifying by the recording device the small change in the length of the muscle. (Otto Frank, *Zeitsch. biologie,* 14.)

The Sensitiveness of the Heart Muscle to Increase in Diastolic Filling—If the resistance against which the heart contracts is increased as by partially occluding the aorta, a compensation of car-

diac output will occur which will eventually result in an unchanged arterial blood pressure. It was formerly thought that this compensation represented a response on the part of the heart to an increase of tension, but the increased output of the heart under these conditions has been found to be always associated with an increased capacity of the ventricle, with, in other words, a dilatation of the ventricle and increased diastolic filling. It is found, however, that this dilatation of the ventricle is not accompanied with an increase of intraventricular pressure during diastole. In fact, the intraventricular pressure may be approximately zero at the end of diastole, whether the heart is beating against 80 mm. pressure or 120 mm. pressure. When, however, the heart is required to meet the demands of a higher arterial pressure, it does so at an increased systolic pressure in order to force the normal quota of blood out through the aorta. It then meets the increased aortic pressure by an increased systolic force exerted upon an increased quantity of blood within it. (Fig. 70.) The increased quantity of blood contained within it, however, does not mean that the fibers of the heart muscle are subjected to an increased tension, but are only increased in length. The increased response of the heart to the increased resistance by an increase of the length of its fibers is a function of the cardiac muscle and is the determining factor in its ability to respond to increased demands upon it.

Effect of Temperature on Heart Muscle—A rise of temperature will increase the frequency of the heart beat. The mammalian heart will beat four times as frequently at 40° C. as at 15° C.

Various salts produce a stimulating effect on heart muscle. For any continued contractions to take place it must be surrounded in a fluid of an osmotic pressure equal to that of the blood. The excised apex of the tortoise heart will not contract, but immersion of its isolated apex in sodium chlorid solution will cause it to contract rhythmically for a long time. It finally stops in a condition of relaxation. The addition now of a trace of calcium chlorid to the solution will again cause contractions for a time. This time the heart ceases to beat in a contracted state. Again the apex can be made to beat by adding a trace of potassium chlorid or phosphate and it will continue beating for many hours. The first effect of the potassium salts has been to produce relaxation of the contracted *apex.*

The Effect of Changes in the Reaction of the Blood and of Varying Percentages of Carbon Dioxid upon the Action of the Heart—Perfusion of the heart with weak acids produces a decrease in the tonus of the heart. The contractions are less forcible and extensive and finally disappear. Weak alkalis produce the opposite effect. The collection of excessive quantities of carbon dioxid will produce the same effect as weak acids. There is unquestionably a mean between alkalinity and acidity which is most favorable to the action of the heart. In so far as carbon dioxid concerns this optimal mean is represented by 5–6 per cent. of an atmosphere of CO_2. The decrease of tonus, accompanied by dilatation of the ventricle and impaired contraction, is represented by Fig. 71.

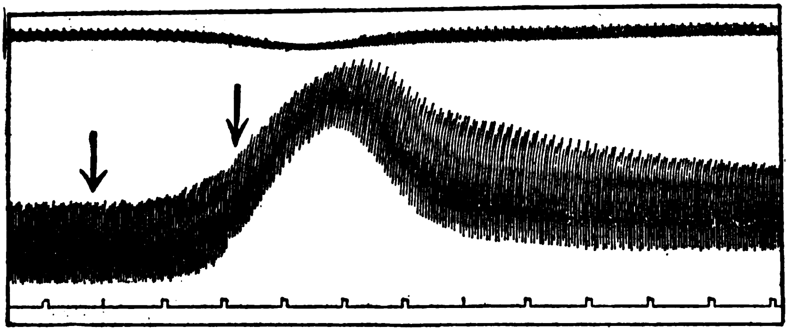


FIG. 71.—VOLUME CURVE OF VENTRICLES (CAT; LOWER CURVE).

The upper curve is the arterial pressure, maintained by an adjustable resistance at 130 mm. Hg. Between the arrows the air used for artificial respiration was replaced by a mixture containing 20 per cent. CO_2 and 25 per cent. oxygen. Note the dilatation with impaired contraction, followed by increased amplitude of contraction. Each down stroke in lower curve represents ventricular contraction. (Starling.)

The Nutrition of the Heart—The heart is nourished by the circulation of blood through the coronary arteries. These arteries terminate in capillaries which supply all parts of the heart muscle. The coronary arteries do not anastomose with each other. They are, therefore, called terminal arteries. Any obstruction to the flow of blood through a branch of a coronary artery, as, for instance, a blood clot, will cause the death of a certain section of heart muscle. The effect of such an accident is almost immediate. This portion of the heart becomes non-conductive. The heart continues beating for one or two minutes; then a beat is occasionally

dropped, and finally the heart stops altogether. At the time when the heart stops it passes into a state of fibrillar contractions, often called delirium cordis, in which state various portions of the heart contract more or less rhythmically without coordination or any sequence. It becomes incapable of carrying on the circulation. A collection of the metabolites resulting from cardiac activity will increase within certain limits the flow of blood through the coronary arteries. Thus the flow of blood through the coronary arteries has been increased from 56 cc. per minute to 180 cc. during a period of asphyxia before the heart failed. The heart therefore contains within itself a mechanism for assisting in the getting rid of the deleterious products of its own activity and of the activity of other muscles. These metabolites are not alone carbon dioxid, because it is impossible with this gas alone to produce the increased flow of blood which is observed in asphyxia.

The Nervous Control of the Heart's Action—In order that the heart may meet the varying needs of the body for a more rapid or slower circulation it is necessary that some mechanism should exist which is capable of producing changes in the action of the heart in response to messages from various portions of the human body. Such changes are also quite as necessary for the sake of the heart itself, in order that it may protect itself, in the presence of excessive demands on the vascular system, against an activity which would quickly exhaust it.

The Nerve Supply of the Heart—The heart receives nerves from the vagus nerve and from the sympathetic nerves. The cardiac nerves of the vagus are axons of cells underlying the ala cinerea of the floor of the fourth ventricle. They leave the trunk of the vagus nerve in the neck and pass as medullated fibers to the heart, where they end around the cells of Remak's ganglion. Non-medullated fibers, the axons of the cells of Remak's ganglion, continue the impulses onward to the cardiac muscle.

In the dog the sympathetic cardiac nerves leave the spinal cord in second and third dorsal nerves (upper fourth or fifth dorsal nerves in the human being). They pass as white rami communicantes to the corresponding thoracic ganglia, and through these to the stellate ganglion. Here they end around cells the axons of which are non-medullated fibers and continue the impulses onward through the inferior cervical ganglion. From these two ganglia the

stellate ganglion and the inferior cervical sympathetic ganglion, and in man from the superior and middle cervical ganglia as well, the nerves pass as non-medullated nerves to the heart. It is possible by the nicotin method to identify exactly the situation of the ganglionic cell station of these nerves.

The Effect of Division and Peripheral Stimulation of the Vagus Nerve—What impulses are transmitted to the heart by the vagus nerve? Stimulation of the divided peripheral vagus nerve will cause the heart to become slower, and in consequence of increased diastolic filling more forcible. If the stimulation is continued the heart will stop altogether. (Fig. 72.) Due to the slowing of the heart, the blood pressure falls. After the cessation of the stimulus the heart will begin to beat again, and harder than ever. So also the blood pressure may rise above normal. These reactionary effects are due to the collection of carbon dioxid in the blood. The

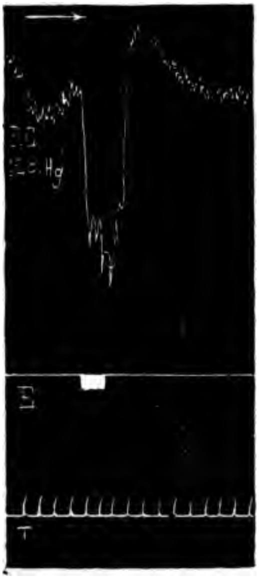


Fig. 72.—Arrest of the Heart of a Rabbit Produced by Stimulation of the Peripheral End of One Pneumogastric.

At P.C. the carotid blood pressure was 12 cm. of Hg. E indicated application of stimulus of an induced current, time indicated by lowest tracing in 2 seconds.

carbon dioxid also stimulates respiration, an effect which also aids the circulation in the manner previously explained.

If the stimulation of the peripheral end of the vagus is not too strong even during the period of stimulation, the heart may begin to beat again. Such a recovery is spoken of as an escape of the heart from the influences of the vagus. During such an escape, however, the cardiac contractions are purely ventricular in character. Any normally augmentatory factor, as an increase of diastolic filling of the ventricle, will favor this escape. The slowing of the heart will increase the diastolic period and, therefore, the filling of the ventricle and in consequence the cardiac output.

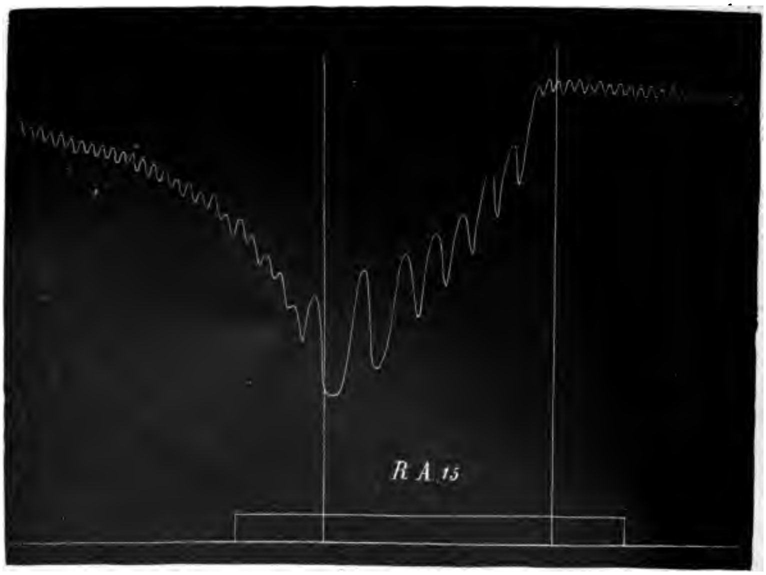


Fig. 73.—The Effect on the Blood Pressure Curve of Stimulation of the Vagus Nerve.

The tracing is to be read from left to right. The period of stimulation is indicated by the vertical lines. (Robert Tigerstedt.)

The Different Effect Exerted through the Vagus upon the Heart When Its Impulses Act upon the Sino-auricular Node or Directly upon the Auricles—The vagus may either affect the heart through the region of the heart which contains the sino-auricular node or act on the auricles directly. In the former case the rhythm

of the heart is (S. venosus) slowed (Fig. 73) while in the latter instance the rhythm is not affected, but the auricular contractions are much weaker. The auricular contractions may be so reduced that they cannot be recorded. As long, however, as there is any contraction in the auricles the rhythm of the ventricles will coincide with that of the auricles. Generally stimulation of the peripheral end of the vagus will cause an entire cessation of the auricular contraction. In this case the ventricles also cease beating. Not infrequently the ventricles will begin beating again after a pause and with a slow, apparently with an independent, rhythm of their own.

Evidence That the Vagus Directly Affects the Muscular Tissue of the Ventricles—When under the conditions described in the last paragraph the contractions of the ventricles again begin they may inaugurate a reversal beat in the heart; and this fact shows that the ventricles are inaugurating their own contractions. It is probable that in the mammalian heart the vagus produces some slight direct effect on the ventricles, because stimulation of the vagus produces a temporary cessation of the ventricular contractions, while functional separation of the ventricle from the auricle produces no such temporary stoppage. The vagus at other times may affect the auriculo-ventricular bundle, producing a block. The auricles may then beat faster than the ventricles.

To sum up, the vagus contains fibers which produce an inhibitory action on the sino-auricular node. This is the most important function of the vagus and effects the rhythm of the heart alone. It also contains fibers acting on the auricles and on the ventricles themselves. These effects are limited to the strength of the contractions.

The effect upon the heart through the vagus is a direct one upon muscular fibers themselves, and not a result of any independent activity of the cells of Remak's ganglia.

Many facts support this view, among them the following:

1. A weak tetanizing current applied to the heart will cause a relaxation (inhibition) of the heart muscle between the points of application of the electrodes.

2. Nicotin will prevent the effect upon the heart ordinarily caused by a peripheral stimulation of the vagus nerve.

3. The usual effects upon the heart from stimulation of the

vagus nerve may be produced whether the pre- or postganglionic fibers are stimulated.

4. Muscarine, a drug which stimulates the inhibitory fibers of the vagus, produces weakening of the heart when painted in solution either on the auricle or ventricle.

The Essential Nature of Such an Inhibitory Process—The essential nature of an inhibitory process has been explained in two ways.

According to one view it is simply a prolongation of the period of rest. The assumption is justified that anabolic changes occur in every tissue during rest. Certainly activity is associated with tissue disintegration or katabolism, and when activity is over a building up process or replacement of the broken down products must occur. This building up, or anabolism, must leave the tissue with more potential power after the inhibitory periods as experiments demonstrate it to have. At any rate, as long as anabolism is taking place the tissue cannot be active.

According to the second view the inhibitory impulses actually stimulate or produce anabolism within the tissues. Inasmuch as every activity of a tissue or every katabolic change is associated with an electrical change of such a character that the point of greatest activity becomes negative, we would expect that inhibition would be accomplished with a difference of potential of the opposite character, and, as a matter of fact, during inhibition the point of reception of the inhibitory impulses becomes positive to other points. There is, in other words, an increase of the resting or demarcation current.

The Activity of the Vagus Mechanism During the Normal State—During the normal state of any animal tonic or constant inhibitory impulses are constantly descending the vagi nerves to the heart. This fact is demonstrated by the increase of frequency of the heart beat which follows the division of both vagi nerves. This effect varies much with different animals. Morphin will augment these constant inhibitory impulses.

Action of Adrenalin upon the Heart—In connection with a description of the cardiac functions of the vagus nerve it is desirable to consider the action of adrenalin upon the heart. The blood normally contains a definite quantity of this substance, and it possesses an important stimulant action upon the heart which is identical

with the effect produced by stimulating the sympathetic nerves. Whereas, however, adrenalin produces a contraction of all vessels in the body supplied with sympathetic fibers, it produces a dilatation of the coronary vessels, serving, therefore, admirably in virtue of this associated action to increase the rate and force of the heart beat.

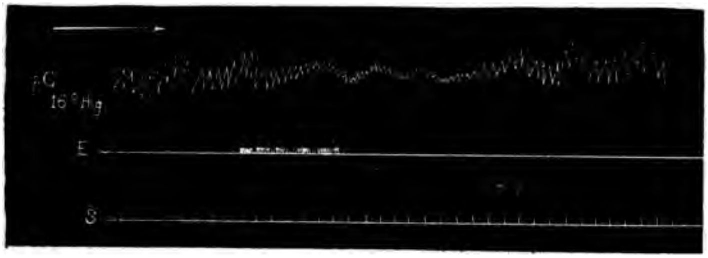


FIG. 74.—INCREASE IN THE FREQUENCY OF THE HEART BEAT FOLLOWING STIMULATION OF AN EFFERENT BRANCH OF THE FIRST THORACIC SYMPATHETIC GANGLION.

Experiment on a curarized dog.

PC, carotid blood pressure; E, period of stimulation of the nerve by an induced current; S, time in seconds. (Elgley.)

The Function of the Cardiac Sympathetic Nerves—The Effect of Peripheral Stimulation—*The Action of the Sympathetic Cardiac Nerves*—The sympathetic cardiac nerves are the normal antagonists of the vagi. Peripheral stimulation of the sympathetic nerves will increase the frequency of the heart beat. Usually the strength of the auricular and ventricular contractions is also increased. (Figs. 74 and 75.)

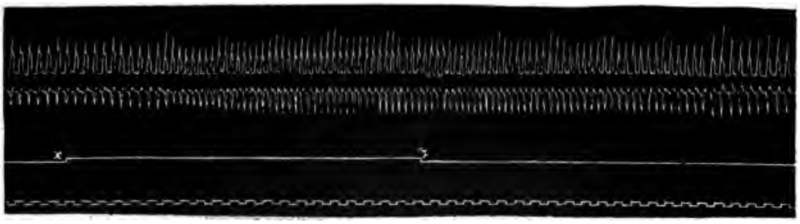


FIG. 75.—TRACING OF VENTRICULAR (UPPER CURVE) AND AURICULAR CONTRACTIONS (LOWER CURVE).

From *x* to *y*, the accelerator nerves stimulated. Lowest line = seconds. (Starling.)

The Combined Effects of Peripheral, Vagus and Sympathetic Stimulation—While the latent period of the effect of vagus stimulation on the heart is only one or two seconds, the latent period of the sympathetic stimulation is 10, or even 20, seconds. When, therefore, both nerves are peripherally stimulated the first effect would be a vagus effect, which becomes fatigued about the time that the sympathetic effect come on. (Figs. 76 and 77.) Like the vagus, the sympathetic nerve produces an augmentative influence on the heart. Excision of the stellate ganglion causes slowing of the heart.

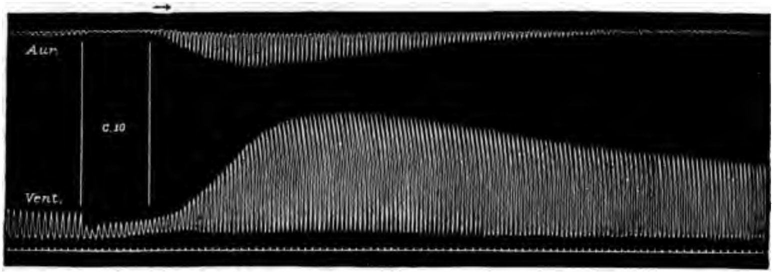


FIG. 76.—TRACING TO SHOW THE PRIMARY INHIBITORY EFFECT AND SECONDARY AUGMENTATORY EFFECT UPON THE BEATS OF THE AURICLES AND VENTRICLES OF THE FROG'S HEART, OBTAINED BY STIMULATING THE VAGOSYMPATHETIC NERVE IN THE NECK.

The rate is unaltered. Suspension method with the clamp in the auriculoventricular groove.

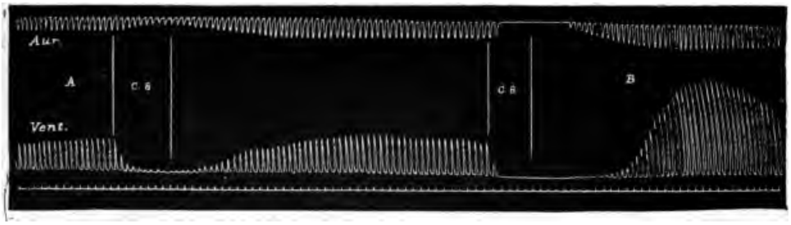


FIG. 77.—TRACING OF HEART-BEAT OF FROG.

Suspension method clamp in auriculoventricular groove. Stimulation of the vagus in the neck (i.e., the combined vagus and sympathetic nerve), showing the effect of the simultaneous stimulation of the two nerves, namely, a primary complete inhibition followed by augmentation. (E. A. Schäfer.)

The Afferent Channel for the Nervous Impulses Affecting the Heart and the Cardiac Center—*The Afferent Channel*—The vagus

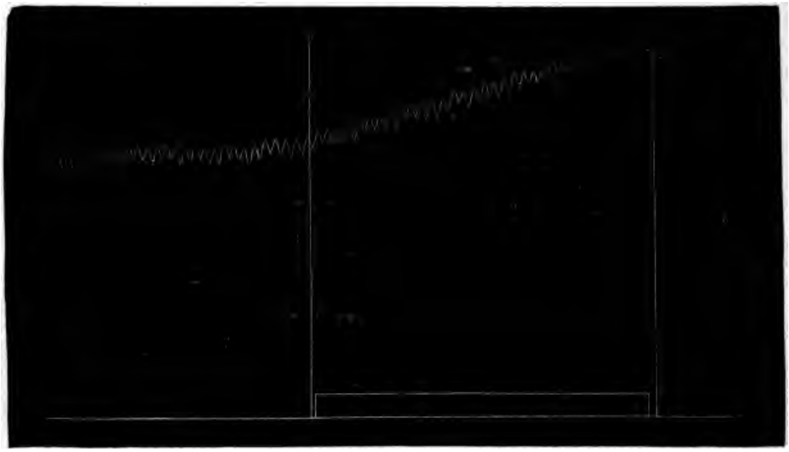


FIG. 78.—REFLEX FALL OF PRESSURE AFTER STIMULATION OF AN AFFERENT MUSCULAR NERVE IN A RABBIT.

The tracing is to be read from right to left. The duration of the stimulus was 10 sec. and is indicated by the raised horizontal line joined at its ends to the base line. (Robert Tigerstedt.)

and sympathetic nerves to the heart are only half of the mechanism for the regulation of the heart's activity. The other half concerns the afferent channels.

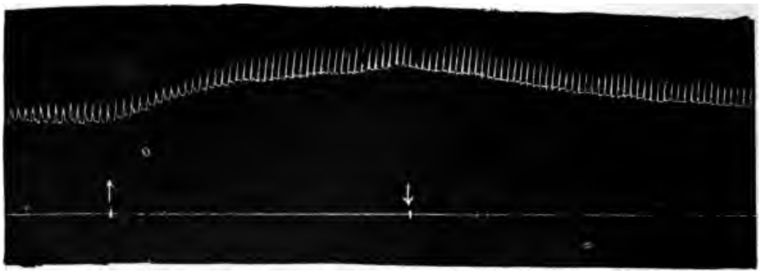


FIG. 79.—BLOOD-PRESSURE CURVE FROM CAROTID OF DOG.

Between the arrows the central end of a sensory nerve was stimulated. (Starling.)

In other words, the heart's action cannot change to meet varying conditions in the body without provision for the transmission of afferent impulses from other regions of the body into efferent *impulses. (Figs. 78, 79* and 80.) Unquestionably the common meet-

ing place of these impulses is in the medulla; the efferent vagus fibers to the heart are axons of cells in the ala cinerea of the floor of the fourth ventricle.

Though the sympathetic fibers are axons of cells in the lateral horn of the spinal cord of the upper dorsal region, these cells are unquestionably directly under the control of the medullary centers.

The most important afferent cardiac nerves run to the medulla in the vagus nerve from the heart itself and the aorta. In the mammalian heart fibers can be seen upon the surface of the ventricle. Stimulation of their central end produces any one of the following results:

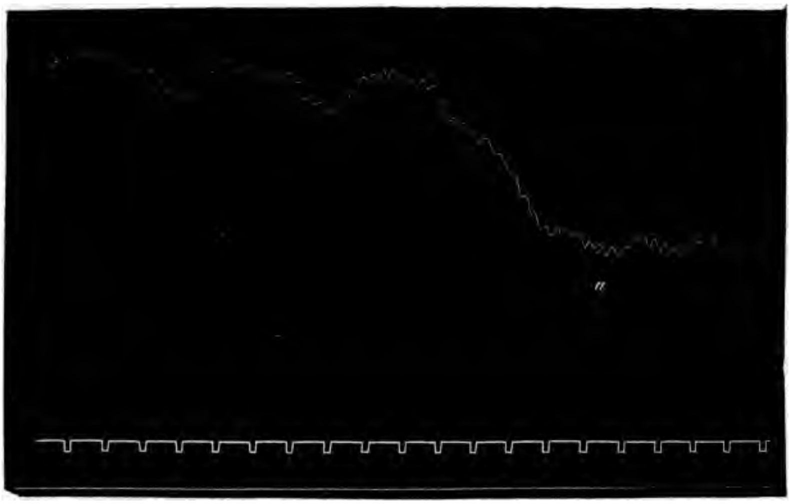


Fig. 80.—**Reflex Increase of Blood Pressure in Rabbits Produced by Irritation of the Skin.**

Tracing is to be read from right to left. (Robert Tigerstedt.)

1. Slowing of the heart.
2. Rise of blood pressure from constriction of the splanchnic area.
3. Fall of blood pressure due to dilatation of the arteries of the body.

Pathological lesions of the heart may be accompanied with pain. The heart, therefore, is supplied with sensory nerves.

A. The Depressor Nerve—In the rabbit these depressor fibers

form two separate nerves coming off from the trunk of the vagus and the superior laryngeal nerve. It runs up to these portions of the vagus from the cardiac plexus of nerves.

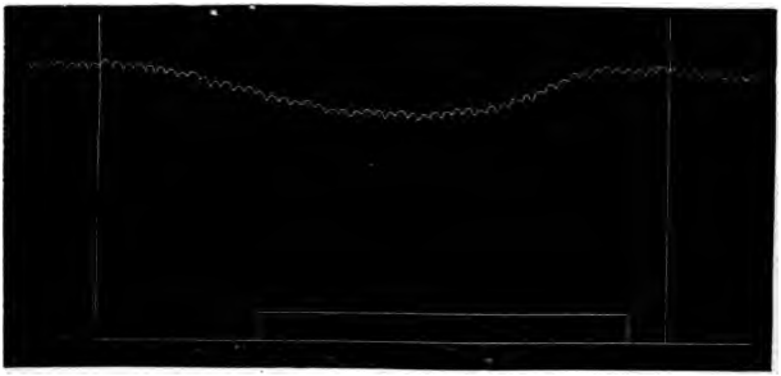


FIG. 81.—THE BLOOD PRESSURE CURVE AFTER ELECTRICAL STIMULATION OF THE DEPRESSOR NERVE.

The tracing is to be read from right to left. The period of stimulation is indicated by elevated horizontal line joined by two vertical lines to the base line. The period lasted 10 sec. (Robert Tigerstedt.)

B. The Afferent Paths for "Depressor" Impulses—Stimulation of its peripheral end is without effect, but stimulation of its central end produces a great fall of blood pressure. (Figs. 81, 82, and 83.)

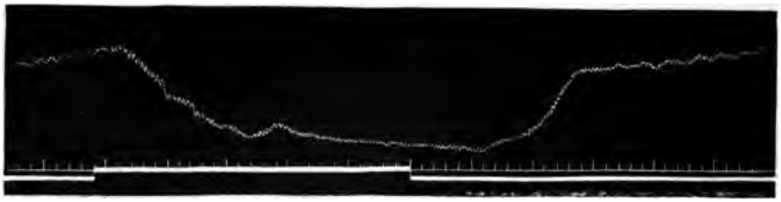


FIG. 82.—EXCITATION OF THE CENTRAL END OF THE DEPRESSOR NERVE OF RABBIT.

Fall of blood-pressure due to reflex relaxation of the splanchnic vessels. (N.B. The vagus was uncut, hence the fall is associated with reflex slowing of the heart-beat. The abscissa has been raised 3 cm.) (Waller.)

C. The Efferent Paths of the Depressor Nerve and the Two Factors Concerned in the Depressor Effect—This fall of blood pressure is caused by the stimulation of two kinds of efferent impulses

resulting from the afferent impulses passing to the medulla along the depressor nerve.

One kind of efferent impulse descends through the cardiac vagus nerves and causes a slowing of the heart. These are prevented by a section of the vagi. The other kind descends to all the blood vessels of the body, causing a universal vascular dilatation, especially of the splanchnic area.

D. The Peripheral Termination of the Depressor Nerve and the Significance of Such an Ending—The cardiac plexus to which this nerve runs is in intimate relation to the aorta. Any increase of pressure in the aorta is capable of stimulating the depressor nerve so that it forms one of the important means by which the heart may be relieved of excessive pressure. Currents of action have been detected in this nerve when the aortic pressure is high.

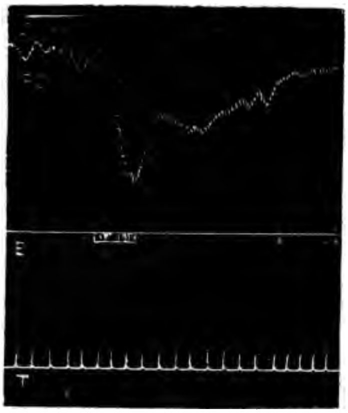


Fig. 83.—Tracing of the Arterial Pressure as Effected by Stimulation of the Central End of the Depressor Nerve in a Rabbit.

Time in 2 sec. (E. Grey, "Traite elementarie de physiologie.")

The Nature of Other Afferent Paths in the Vagus Nerve—Other afferent nerves ascend to the medulla through the vagus which are related to the cardiac reflexes.

Stimulation of the central end of the vagus generally causes a slowing of the heart's action. Many of the fibers responsible for this effect have their peripheral termination in the lungs.

Inflation of the lungs is said to cause an acceleration of the

heart's action. Whether these afferent impulses cause an inhibition of the vagus or a stimulation of the sympathetic is not known.

The Relation of the Rate of the Heart to Blood Pressure—Of great importance is the definite relation of blood pressure to the rate of the heart beat. The blood pressure with few exceptions, as during exercise, varies inversely as the heart rate. All the paths of this reflex are not known.

The Effect of Exercise on the Heart Beat and on Blood Pressure—Muscular exercise increases the rate and force of the heart beat and the blood pressure.

The following factors are the cause of these two changes:

1. The effect of increased carbon dioxid and lactic acid on the blood vessels and these and other metabolites on the coronary circulation.

2. An increase in the frequency and force of respiration.

3. An increase in the return of the blood to the heart, due to the contractions of the voluntary muscles.

4. Through attention there results a reflex effect from the cortical centers upon the medullary centers which results in a rise of the blood pressure by a contraction of the splanchnic area, and the rise bears a direct relation to the injurious effects of exercise after eating.

5. The increased secretion of adrenalin.

6. The blood pressure is also raised by the action of the carbon dioxid on the medullary vasomotor center. Within the contracting voluntary muscles the vessels are dilated. It is also possible by means of central reflexes through the cardiac center in the medulla that the primary inhibitory effect upon the vasomotor center through the vagus during exercise may be switched off upon the accelerator efferent nerves so that reflexly the heart becomes more rapid in force and frequency.

7. Some accelerator effect depends upon the rise of body temperature.

Explanation of Second Wind—After exercise has been in progress the first sense of exhaustion is followed by relief. This relief is called second wind. It depends upon the following factors:

1. Dilatation of the vessels in the contracting muscles, due to the discharge of metabolites in them.

2. A diminution in the respiratory quotient; more oxygen is

taken in by the body in proportion to the carbon dioxid given off from the body.

3. An improvement in the coronary circulation and a response by the heart, in virtue of its power of accommodation to the increased blood pressure. The heart always responds to a higher blood pressure. As the blood pressure rises by successive steps the heart maintains the same output. Fig. 84.

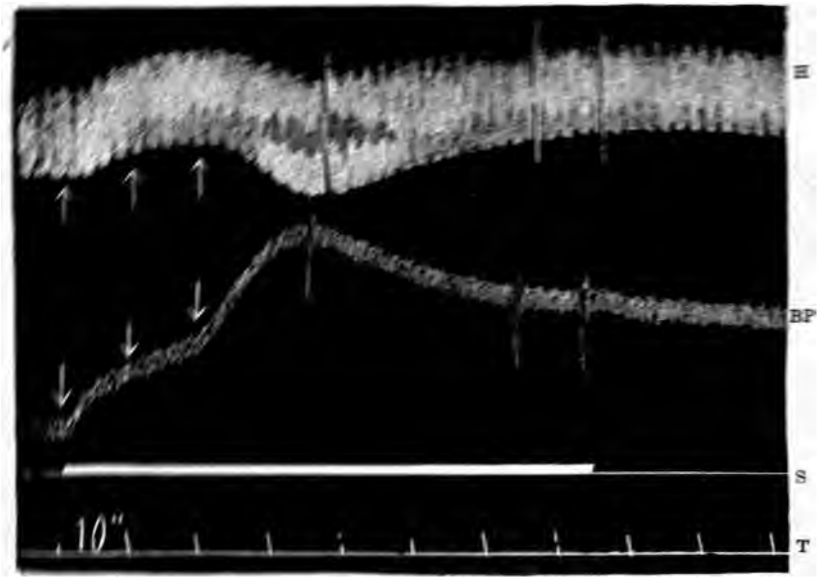


FIG. 84 CURVE SHOWING THE EFFECT OF A SUDDEN RISE IN THE ARTERIAL RESISTANCE ON THE OUTPUT AND VOLUME OF THE VENTRICLES.

Systole causes a downward movement of the lever of the cardiometer. H, heart volume; BP, arterial blood-pressure; S, signal showing duration of stimulation of splanchnic nerve; T, time-marker, 10 sec. (Starling.)

Nervous Control of the Blood Vessels—The Necessity for Its Existence While an increase in the force and frequency of the heart will supply more blood to the general capillaries of the body, such a means of furnishing more blood to actively functionating tissues as the muscles or glands is totally inadequate. Some means must exist for increase of the blood supply to those organs where it is most needed without interfering with the general blood supply to the body at large. During active muscular exercise the me-

tabolism of the whole body may be increased five to six times. Most of this increased metabolism is going on in the muscles. A provision exists for taking the blood from, for instance, the digestive system where it is not needed and increasing the flow through the muscles where it is most needed. This change in the distribution of the blood is chiefly accomplished through the nerves which supply the walls of the blood vessels. It is in part accomplished through local chemical changes.

The Portion of the Nervous System Responsible for the Control of Blood Pressure—That portion of the nervous system which is chiefly concerned in the control over the distribution of the blood in the body is the sympathetic nervous system.

THE SYMPATHETIC NERVOUS SYSTEM

The sympathetic nervous system consists of a chain of ganglia connected with each other and lying parallel to the vertebral column. There is in general a ganglion for each spinal nerve, at least in the dorsal and lumbar region of the spinal cord. In the cervical region the ganglion corresponding to each spinal nerve is collected into three ganglia, the superior, middle and inferior cervical ganglia. The inferior cervical sympathetic ganglion is connected by two cords, which surround the subclavian artery, with a large ganglion below the subclavian artery, which is called the stellate ganglion. The ring formed by the two cords surrounding the subclavian artery is called the ansa or annulus of Vieussens.

These various ganglia receive nerves which are branches of the anterior spinal nerves from the first dorsal to the third or fourth lumbar, and are all connected to each other by a double cord. The stellate ganglia receive branches from the upper fourth or fifth dorsal nerves. Many of these are continued through into the superior middle and inferior cervical ganglia.

The nerves connecting the anterior spinal nerves with the sympathetic ganglia are called rami communicantes. They are of two kinds, gray and white rami. The white rami are medullated, while the gray are not. The white rami represent those nerves which are axis cylinders of nerve cells in the lateral portion of the gray matter of the spinal cord near the level of the anterior root, with

which the white rami emerge from the cord. All white rami end around some of the ganglion cells of the sympathetic system. The impulses of the white rami are continued on by the axons of the ganglionic cells. These axons are always non-medullated; they are called postganglionic fibers. The gray rami are simply postganglionic fibers which have rejoined the spinal nerves to issue at a different level. We have already described the branches of the sympathetic nerves to the heart.

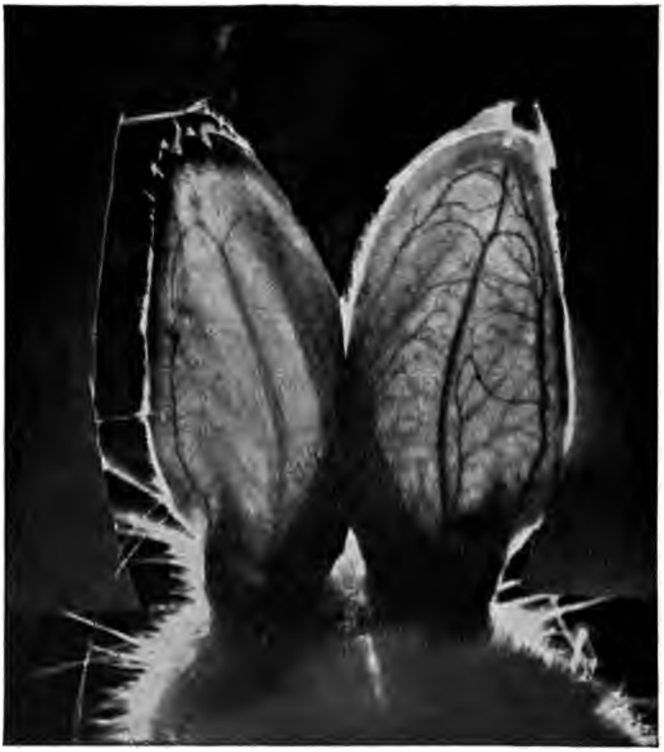


FIG. 85.—SHOWING THE INCREASED VASCULARITY IN THE RABBIT'S EAR PRODUCED BY DIVIDING THE SYMPATHETIC NERVES TO THE RIGHT EAR.

(This animal was in shock at the time of the division.)

Effect of Peripheral Stimulation—When these nerves are stimulated the blood vessels which are supplied by them contract. The noted experiment which demonstrates their function consists in

the division of the cervical sympathetic of a rabbit on one side of the neck. Immediately the vessels of the head and neck, but particularly those of the ear, because they show the changes so well, will dilate. (Fig. 85.) Vessels in the ear which were previously invisible become now visible and the whole ear redder. If now the peripheral divided end is stimulated, the vessels of the ear once more contract. This experiment demonstrates clearly that the sympathetic nerves carry vasoconstrictor impulses to the blood vessels.

The Normal Starting Place of Vasoconstrictor Impulses—Do these impulses originate in the cells of the spinal cord, from which the white rami of the sympathetic system originate, or higher up? We can only decide by dividing the cord at a higher level. Let us divide the cord at the level of the first dorsal nerve. Immediately following this section there will be a great fall of arterial blood pressure throughout the body. It may even fall from 120 mm. of Hg. to 40 or 50 mm. Hg. The heart will beat more rapidly in an attempt to compensate for the fall of blood pressure, so that the low pressure is entirely due to the loss of vasomotor impulses, which normally are constantly passing along the sympathetic nerves to the blood vessels.

These impulses, therefore, must originate somewhere in the nervous system above the spinal cord. If the upper extremity of lower segment of the divided spinal cord is stimulated the blood pressure will rise once more.

If now we divide the brain above the medulla oblongata there will be no fall in blood pressure. The vasoconstrictor impulses must, therefore, originate in the medulla oblongata. Moreover, their exact site of origin in the medulla can be identified with a region in the floor of the fourth ventricle lateral to the middle line and on a level with the origin of the facial nerve. This region represents the continuation forward of the lateral columns of the spinal cord after the pyramidal tracts have left the lateral columns to form the decussation of the pyramids. A destruction of this region of the medulla will cause the same general fall in blood pressure. This region is called the vasomotor center.

Significance of the Term Center, as Applied to This Starting Place—The use of the term center, however, must not be construed to mean a region which originates vasoconstrictor impulses. It is

such is the case may be easily proved by excising the heart quickly, when it will again begin to beat, or by beginning artificial respiration while the blood pressure is falling. As soon as the heart is once again supplied with oxygen it will begin once more to contract, even though the blood pressure would have risen still higher. To what is the rise in the blood pressure during asphyxia due? It is due to the lack of oxygen or to the excess of carbon dioxid.

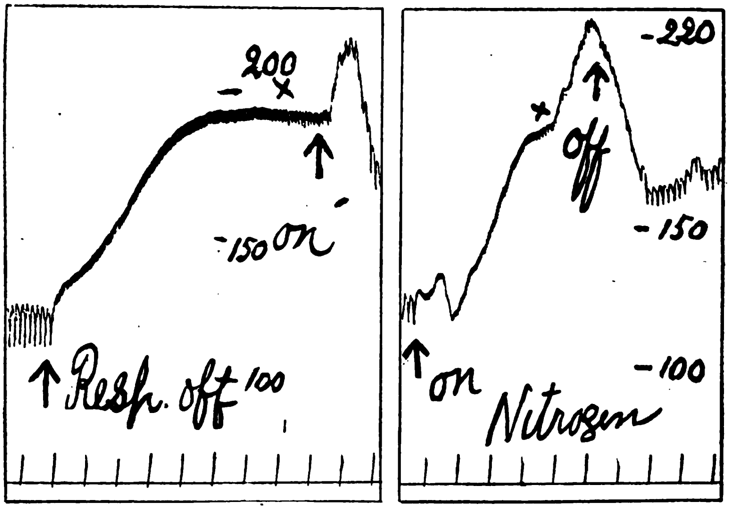


FIG. 86.—IN THIS AND THE FOLLOWING EXPERIMENT THE CAT WAS DECEREBRATED BY A DIVISION OF THE BRAIN STEM JUST ABOVE THE ANTERIOR CORPORA QUADRIGEMINA, BOTH VAGI WERE CUT AND THE ANIMAL CURARIZED.

In A simply the artificial respiration was discontinued. There occurs a rise of blood pressure to over 200 mm. of mercury.

The experiment illustrates the effect on the vasomotor center of a combination excess of CO_2 in the blood and an oxygen lack.

N. B. The artificial respiration is continued with pure nitrogen alone.

There occurs quite as high a rise in blood pressure, which in this case depends alone on an oxygen lack.

We must test each separately by respiring an animal in the first place with some indifferent gas such as nitrogen or hydrogen, in which case the animal will suffer from the lack of oxygen, but will rid its blood of carbon dioxid; and in the second place by respiring the animal with carbon dioxid containing a large percentage of oxygen; in which case the animal will obtain sufficient oxygen, but will store up within its blood an excess of carbon dioxid.

Such experiments demonstrate that both a diminution of oxygen and an excess of carbon dioxid will stimulate the vasomotor centers, the effect coming on more quickly when due to an excess of carbon dioxid. (Figs. 86, 87 and 88.)

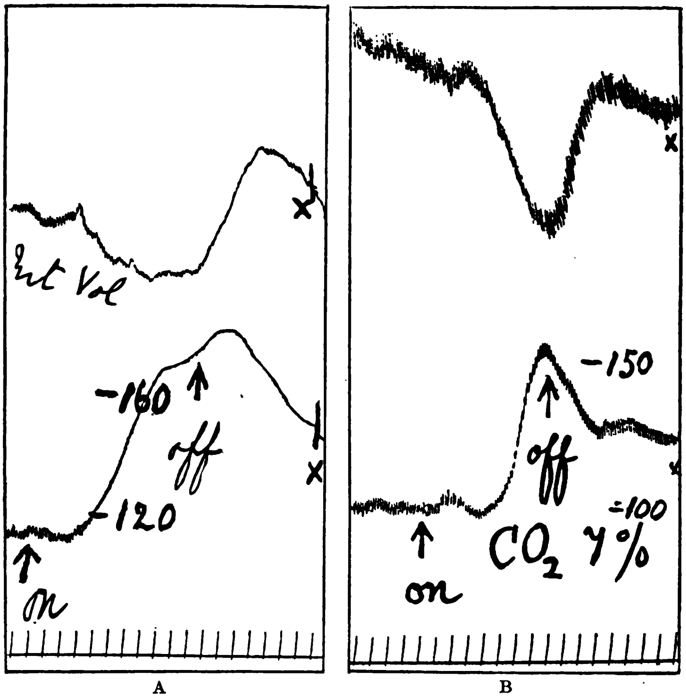


FIG. 87.—SAME PREPARATION AS IN THE PREVIOUS EXPERIMENT, I.E., CAT DECEREBRATED, CURARIZED AND BOTH VAGI CUT.

In A artificially respired between the arrows with a mixture of 4.7 per cent. CO_2 and 20 per cent. O_2. The experiment illustrates the effect of an excess of carbon dioxid in the absence of oxygen. The blood rises and the intestinal volume diminishes, but neither to the degree as in the previous experiment.

In B the animal is respired with 7 per cent. CO_2 and 25 per cent. O_2 with little increase in the height to which the blood pressure rose.

Effect of Increase of Lactic Acid on the Vasomotor Center—Another factor must also be considered. Any muscular exertion in the absence of sufficient oxygen is accompanied by the accumulation of lactic acid in the blood. The injection of lactic acid into *the circulation* will of itself cause a rise of blood pressure.

In ordinary asphyxia, therefore, three factors are certainly involved:

1. A diminution of oxygen.
2. An accumulation of carbon dioxid.
3. An accumulation of lactic acid.

All stimulate the vasomotor center.

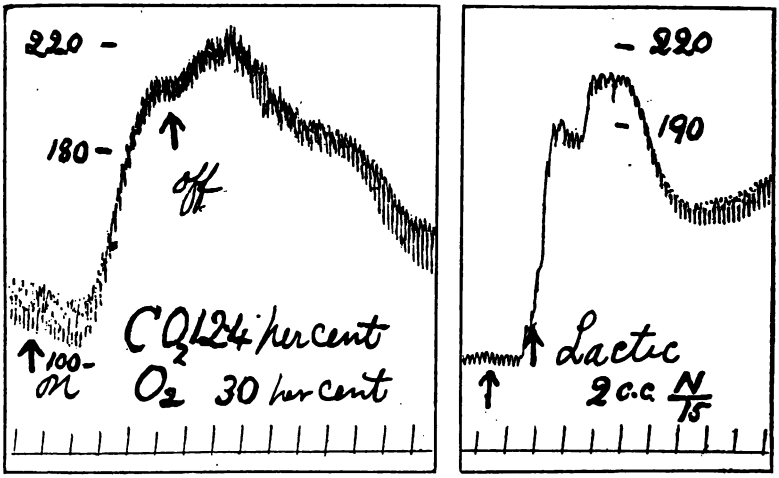


Fig. 88.—In These Experiments the Cat Received the Same Preliminary Treatment, i.e., Rendered Decerebrate, Curarized and Both Vagi Cut.

In A the animal was respired with 12.4 per cent. CO_2 and 30 per cent. O_2. In this animal the blood pressure arose quite as high as in the first asphyxia experiment, so that such excessive amounts of CO_2 are efficient even in the absence of oxygen lack.

N. B. The cat received intravenously 2 cc. of $\frac{N}{15}$ or 6 per cent. lactic acid solution, artificial respiration being continued.

The blood pressure was increased about as much by this procedure as by CO_2 excess or oxygen lack, demonstrating that in all three of these experiments there is a common factor, an excess of the hydrogen ions in the blood, which is responsible for the effect.

The Antagonistic Effect Exerted through the Vagus to Excessive Chemical Effects on the Vasomotor Center—Thus far we have considered the effects of asphyxia on the vasomotor center undisturbed by any other influences upon the heart through the vagus nerve. If the animal is allowed to pass into asphyxia in the same manner by withholding artificial respiration during poisoning

with curare, without a division of the vagus, the same effects will be produced, but they will be more gradual and prolonged.

Through the vagus center the heart will be inhibited. Its action will be slower, and consequently the blood pressure will not rise so rapidly. The final heart failure will be postponed because of its slower action. Two causes act upon the vagal cardio-inhibitory center.

The Two Factors Involved—The first is the accumulation of carbon dioxid. This gas stimulates the vagal cardio-inhibitory center as well as the vasomotor center. Secondly, on account of the increased blood pressure the tension within the unyielding cranial cavity is increased. The increased intracranial pressure further stimulates the vagal cardio-inhibitory center.

The Traube Hering Waves—During the period of increased blood pressure resulting from asphyxia two kinds of waves appear on the blood pressure curve.

One kind of these waves is the respiratory wave. It is formed of elevations and depressions of the blood pressure curve occurring at regular intervals with the pulse wave, and are in part due to increased pulmonary capacity accompanying inspiration, but in the opinion of many are in part due to irradiation of impulses from the excited respiratory center to the vasomotor center in the medulla. (Fig. 89.) Even a single twitch of the diaphragm, insufficient in itself to cause any mechanical effect upon the circulation, may be observed to accompany each rise in the blood pressure curve.

Another kind of wave is the Traube Hering wave. It is repeated more slowly than the respiratory wave, and is due to irregularity of excitation of the vasomotor center during a period within which it is being whipped, so to speak, to its utmost.

The Traube Hering curves are often present after large doses of morphia or accompanying hemorrhage.

The Effect of Digitalis and Strophanthus—Other agents affecting the vasomotor center are drugs. Digitalis and strophanthus both stimulate it.

Vasomotor Impulses of Spinal Origin—The preceding description demonstrates the important functions of the medullary vasomotor center, but are analogous functions possessed by the spinal cells from which the rami communicantes directly arise. We have

seen that a large fall in blood pressure follows a high division of the spinal cord. After, however, one or two hours the pressure will begin to rise. If, on the other hand, the spinal cord of the animal is destroyed, the blood pressure will sink to 0 and the animal will die.

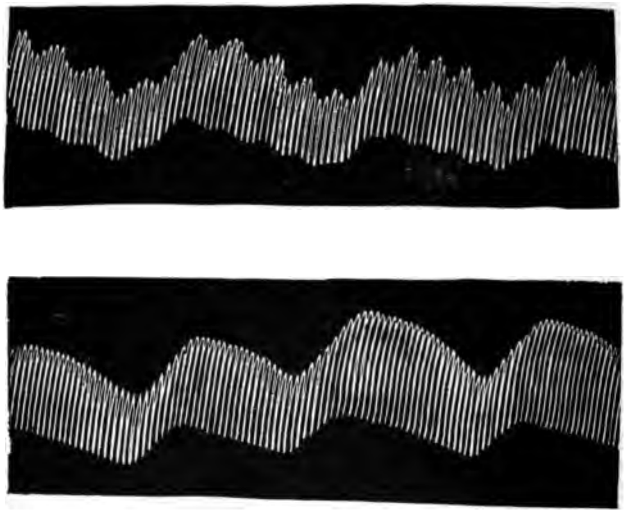


FIG. 89.—BLOOD-PRESSURE TRACINGS, SHOWING CARDIAC AND TRAUBE HERING CURVES.

In the upper tracing made during the continuation of artificial respiration, three curves are present: (1) Those due to the heart beat; (2) those due to respiration, termed respiratory curves; and (3) those due to irregular excitation of the vasomotor center and termed Traube Hering curves by some, and S. Mayer curves by others.

The lower curve is made from a curarized animal just after cessation of the artificial respiration. The cardiac and Traube Hering curves are alone present.

There must, therefore, exist in the spinal cord other vasomotor centers which participate to a certain degree in the maintenance of vascular tone and which are capable of replacing the medullary vasomotor center when the latter cannot functionate. There is no coordination between these centers and those controlling the heart.

The Susceptibility of the Spinal Centers to the Chemical Changes in the Blood—The spinal centers are susceptible to changes *in the composition* of the blood. In the rise of pressure which

follows asphyxia in the spinal animal the main factor is the deficiency in the lack of oxygen. A large excess, however, of carbon dioxid or the injection of lactic acid will produce a rise of blood pressure. (Fig. 90.) While 5 per cent. of carbon dioxid will stimulate the medullary vasomotor center, 25 per cent. of the same gas is required to cause a rise of blood pressure in the spinal animal.

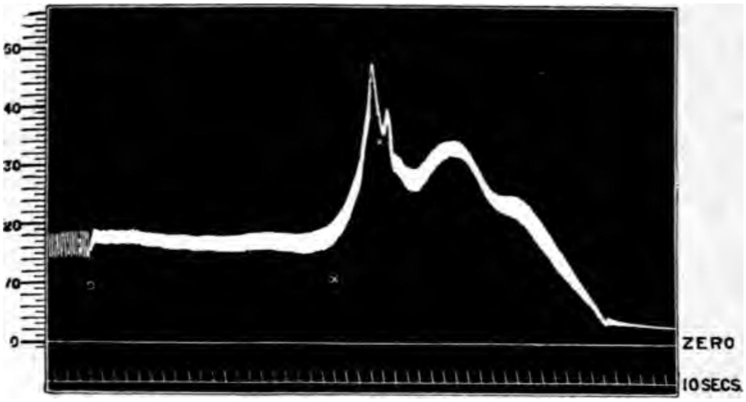


FIG. 90.—BLOOD-PRESSURE TRACING TAKEN BY A MERCURIAL MANOMETER FROM CAROTID ARTERY OF A DOG, THREE HOURS AFTER SECTION OF THE CORD, JUST BELOW THE MEDULLA OBLONGATA.

At *o* the artificial respiration was discontinued. A general spasm of the skeletal muscles occurred between *x* and *x*. The muscles then relaxed, and were flaccid during the rest of the rise of blood-pressure. (Starling.)

It takes two minutes before the rise of pressure which is due to the administration of nitrogen will come on in the spinal animal. In the same manner 2 cc. of a 1/20 normal solution of lactic acid will stimulate the vasomotor center in the medulla, while 5 cc. are necessary to produce a rise of pressure when the spinal centers alone are acted upon.

Local Constrictor Influences in the Vessel Walls—If the sciatic nerve of one leg is divided there will be an immediate dilatation of the vessels of this leg. But in a day or two this dilatation will pass off and the vessels remain in a state of average constriction. There is no proof that this regaining of tone by the vessels is due to a local nervous mechanism. It is far better to ascribe it to an

automatic myogenetic activity of the muscular fibers themselves which compose the wall of the vessels. The local changes in the caliber of the arteries can be determined by ascertaining the volumetric changes by a plethysmograph in conjunction with the arterial pressure. (Figs. 91, 92, 93 and 94.) In connection with local changes in the blood vessels it must never be forgotten that changes in the caliber of the blood vessels in one part of the body, and therefore in the amount of blood which this portion contains, is associated with reverse changes in another part of the body. This is due to the fact that when constriction or dilatation in one set of vessels occurs there is more or less blood to fill the vessels elsewhere. (Fig. 95.) Such other vessels, therefore, dilate or contract from simply the increase or diminution of intravascular pressure.

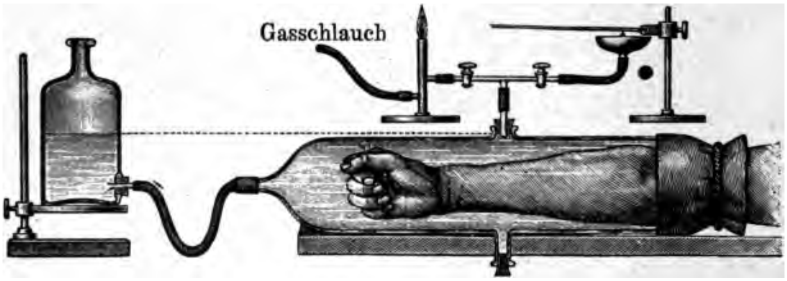


FIG. 91.—PLETHYSMOGRAPHIC METHOD OF TAKING THE CHANGES IN THE VOLUME OF A LIMB AND TWO METHODS OF TRANSMISSION TO THE RECORDING TAMBOUR.

Vasomotor Nerves Producing Dilatation—So far we have considered only the vasoconstrictor apparatus. It can be readily understood that it will be of great advantage to the body to possess a special mechanism for producing dilatation of the arteries, in other words, a double set of nerves equally efficient and opposing each other in their action. Only by the possession of such a mechanism can the organism respond rapidly and accurately to the needs of the body.

The chorda typmani and the nervi erigentes are examples of pure vasodilatatory nerves. (Fig. 97.) Stimulation of its peripheral end will increase the blood flow through the submaxillary gland five- or six-fold.

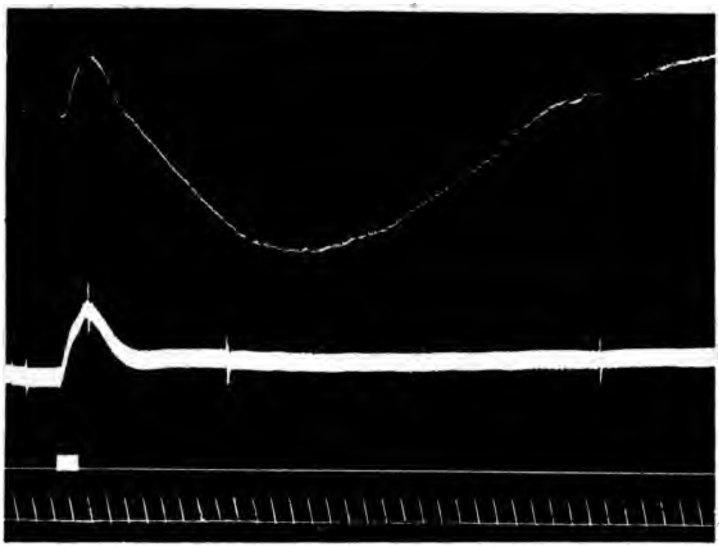


FIG. 92.—EFFECT OF SPLANCHNIC EXCITEMENT ON THE ENERVATED HIND LEG OF CAT.

Upper curve, volume of limb. Lower curve, blood pressure, zero being 45 mm. below excitation marker, which is the upper of the two bottom lines. Time in 10 sec. (N. M. Bayliss, "Reaction of Arterial Wall.")

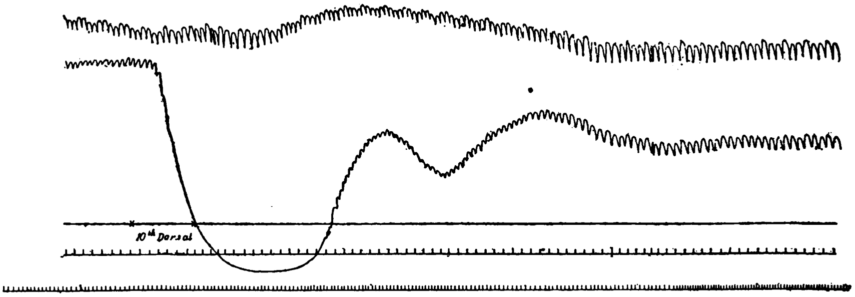


FIG. 93.—SIMULTANEOUS TRACINGS SHOWING THE RISE OF THE CAROTID BLOOD-PRESSURE AND THE FALL IN KIDNEY VOLUME DURING STIMULATION OF THE PERIPHERAL END OF THE DIVIDED TENTH DORSAL NERVE.

Time marking is in seconds and the period of stimulation occurred between the two x x marks. The fall in kidney volume is due to vasoconstriction in the splanchnic area, and the general rise of blood pressure depends upon the damming back of the blood upon the arterial side by the constricted arterioles in the splanchnic area.

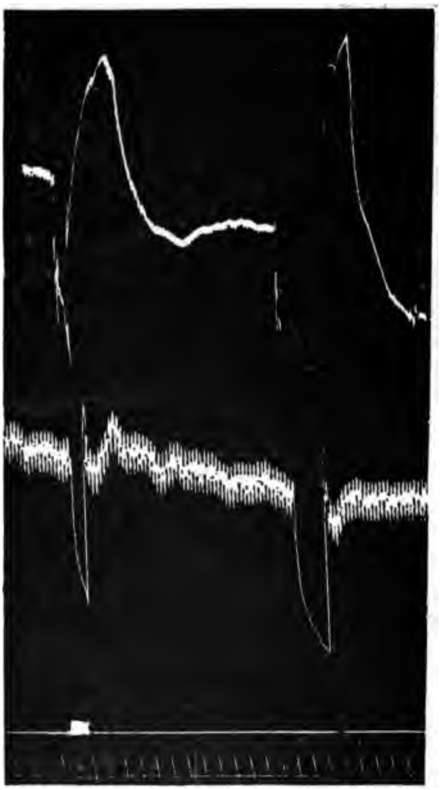


FIG. 94.—EFFECT OF COMPRESSION OF THE ABDOMINAL AORTA ON THE VOLUME OF THE HIND LIMB.

By the compression the blood pressure sinks to 0 and the volume of the hind leg diminishes greatly in size, but upon release of the pressure due to the temporary loss of tone the volume increases greatly at first and then, depending upon the stimulus of the increased intravascular tension to the muscle of the vessel wall, the arteries of the leg constrict, the experiment furnishing an illustration of the compensatory or accommodative power of the local mechanism.

Methods of Measuring Variations in the Circulation through a Portion of the Body—Various means have been adopted to estimate increase of blood flow through an organ.

1. Estimating the increase in redness of an organ.
2. The increase in the volume as measured by a plethysmograph or oncometer and controlled by synchronous blood pressure tracings.
3. In certain organs by their increase in temperature.
4. Increase in the velocity of the blood entering the organ.

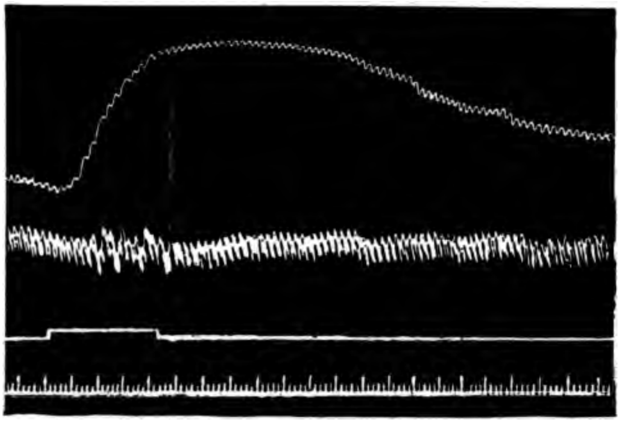


FIG. 95.—EXCITATION OF PERIPHERAL END OF 7TH L. POSTERIOR ROOT.

Uppermost curve, volume of limb; next below, blood pressure; the third line marks period of excitation, and the bottom line time in seconds. Blood-pressure zero 25 mm. below time marker. (N. M. Bayliss, "Vaso-Dilator Fibers.")

5. Increase of the venous outflow by a direct measurement.

The most valuable of these methods is the second. It is necessary, however, to measure synchronously the arterial blood pressure. A plethysmograph can be made of Stent's composition or vulcanite; it must be molded to the shape of the organ. It may be made in two halves or one-half large enough to accommodate the organ, and closed when the organ is within by a glass plate. Room must be left for the vessels and nerves passing to the organ. In Roy's oncometer the two halves are made of metal and hinged together. A bag which may be filled with warm oil surrounds the organ when inclosed in the instrument. Any increase in size of the organ will

displace the oil or air surrounding it. The displaced oil or air operates a recording tambour or float which is in series with the interior of the instrument. Such an oncometer is illustrated in the section on the kidney. Fig. 91 shows a plethysmograph adapted for taking volumetric changes in an extremity.

The Course of the Vasodilators—The course of the vasodilator nerves is quite different from that of the vasoconstrictors. Thus the chorda tympani is a cranial nerve issuing as the nerve of Wrisberg in connection with the seventh nerve. The dilators to the parotid gland issue with the ninth cranial nerve.

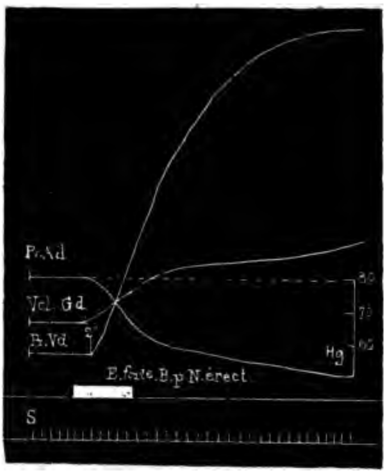


Fig. 96.—The Effect upon the Arterial and Venous Pressures of Excitation of a Vasodilator Nerve. A Dog with a Destroyed Bulb.

Pr. Ad., pressure in the peripheral end of the dorsal artery of the penis; Vol. Gd., volume of the organ; Pr. Vd., pressure in the peripheral end of the dorsal vein of the penis; E, period of excitation of one of the nervi erigentes; S, time in seconds. The size of the vessels entered were too small to transmit the arterial pulsations.

It is probable that most of the dilator nerves have their station peripherally embedded in the organ supplied by them. How many of them pass with the vasoconstrictors to the lower limb is not known. It is probable that the splanchnics convey vasodilator fibers to the vessels of the abdomen. If the constrictor fibers in them have been paralyzed by ergot, peripheral stimulation of the splanchnics will cause a fall of blood pressure.

Methods of Demonstrating the Existence of Vasodilator Nerves to the Lower Limbs—For the purpose of demonstrating the vasodilator fibers to the limbs two procedures are available.

The first method by division of the main nerve or nerves to the region in question and stimulation of these nerves peripherally after two or three days when the vasoconstrictor fibers have degenerated. The vasodilator fibers are still intact at this time. (Fig. 97.)

The second method of demonstrating the vasodilatory fibers is by stimulating the mixed nerve with weak induction shocks repeated at slow intervals only, one to four, or even 16, times per second. (Fig. 98.)

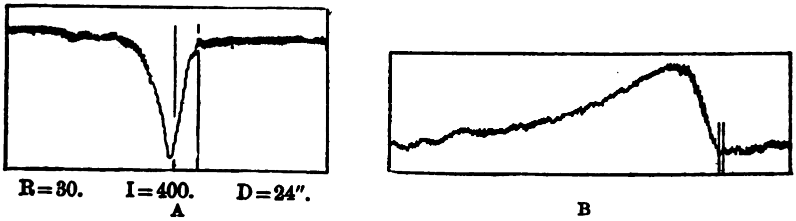
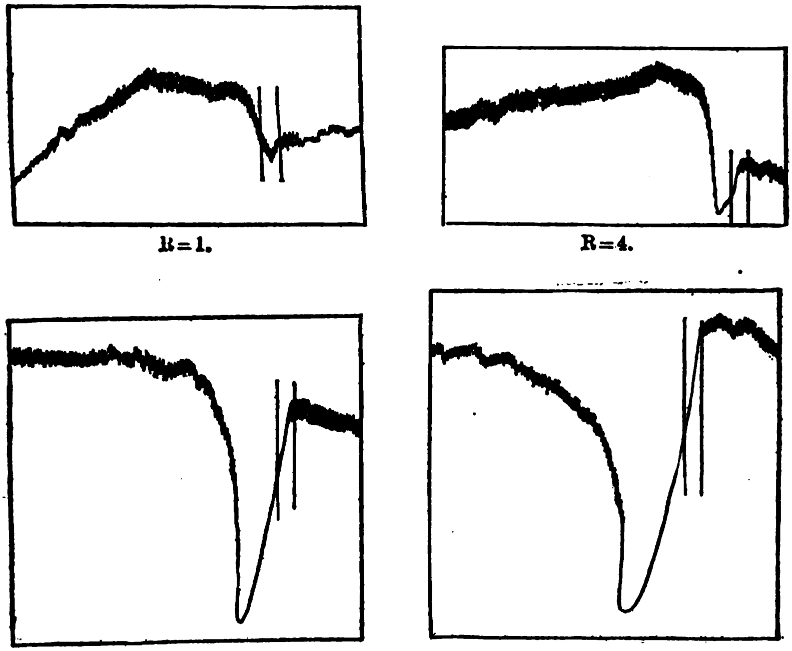


FIG. 97.—TRACINGS INDICATING PLETHYSMOGRAPHIC VARIATIONS OF THE VOLUME OF THE HIND LIMBS WHEN PERIPHERAL END OF THE DIVIDED SCIATIC NERVE WAS STIMULATED.

In A immediately after division, 30 times a second, with an intensity of 400 arbitrary units and a duration of each shock of 1/24 of a second, and in B four days after section. In A vasoconstriction was produced, and in B vasodilatation. (Burditch and Warren.)

The Relation of the Vasodilators to the Postspinal Roots—These nerves pass from the spinal cord through the posterior spinal root instead of the anterior, as is the case with all other efferent nerves. They do not possess a connection in the posterior spinal ganglia. Stimulation of the posterior root both proximal and distal to the ganglion produces the same dilatation. (See Fig. 95.) Consequently the impulses in the posterior root of a spinal nerve pass along the vasodilator fibers in a direction opposite to the usual direction of impulses in the root. The vasodilator impulses are, therefore, spoken of as antidromic impulses. Vasodilatation produced by stimulating them is manifest upon a region far below the level at which the effect from stimulating the corresponding vasoconstrictor nerves results. Vasodilator reflexes may be evoked by

placing mustard or croton oil on the skin or conjunctiva. After such application the area treated becomes red and infected. Section of the posterior root proximately to the ganglion will not prevent this reflex dilatation, but sections distal to the ganglion will do so. It must, therefore, be concluded that the sensory nerves from the ganglion cell of the posterior spinal ganglion passing in a peripheral direction divide some fibers terminating as cutaneous sensory fibers in the skin, while others pass as vasodilator fibers to the walls of the blood vessels. We may term the vasoconstrictor nerves augmentor or motor and the dilator nerves to the periphery, dilator or inhibitory.



R=1. R=4.

R=16. R=64.

FIG. 98.—IN THESE FOUR EXPERIMENTS THE PERIPHERAL END OF THE DIVIDED SCIATIC WAS STIMULATED WITH A CONSTANT INTENSITY AND DURATION, BUT WITH THE DIFFERENT RATES INDICATED WITH A SLOW RATE VASODILATATION RESULTS AND WITH RAPID RATE VASOCONSTRICTION.

Afferent Paths for Vasodilatation—A similar classification may be made of the afferent nerves, though, of course, the tracts are *more numerous and* not so well defined. Those afferent impulses

which raise the blood pressure are called pressor impulses and those lowering the blood pressure are termed depressor impulses. Practically all sensory nerves conveying sensations of pain carry pressor impulses in the absence of consciousness.

The most important depressor nerves are the depressor nerve already described passing from the aorta, and the depressor fibers of the vagus nerve. Both terminate in the vasomotor center. Stimulation of the depressor nerve produces very prolonged effects.

From the brain also important depressor impulses arrive at the vasomotor center. Because this organ is responsible for the life of the centers themselves, it demands to the last a good blood supply.

Fig. 99.—Illustrating the Large Increase of Blood Pressure and of the Excitability of the Vagus Center Due to the Intravascular Injection of Adrenalin.

Rabbit, artificial respiration. Injection of curare. Injection of adrenalin. When the blood pressure is highest the pulse showed the characters of a vagus pulse which became more marked after a division of both vagi nerves.

The Adrenalin Function—A powerful influence in producing vascular changes is adrenalin. This substance is secreted by the medulla of the suprarenal gland. The rapidity of the secretion is under the direct control of the abdominal splanchnic nerves. Injections of adrenalin produce a contraction of the heart, dilatation of the coronary vessels and universal vascular constriction. (Fig. 99.) Accumulations of carbon dioxid, as in asphyxia, lower the tonus of the heart and consequently favor dilatation. It also produces vasomotor constriction. This action is due to the effect of the carbon dioxid on the vasomotor centers. It is, however, associated with stimulation of the splanchnic nerves and, therefore, with the discharge of adrenalin. The action, however, of adrenalin on the heart is opposite to that of carbon dioxid,

and its discharge, therefore, into the circulation during asphyxia is an important conservative factor during period of excessive collection of carbon dioxid in the blood in preventing dilatation of the heart. It must not be forgotten that the constrictor effects of accumulations of carbon dioxid and lactic acid on the nerve centers are also opposed by the local dilator effects of these agents on the blood vessels, an effect which is very marked in the denervated limb.

QUESTIONS AND ANSWERS

Page 4

Q. What are the functions of the blood?

A. See text.

Q. Describe the red cells.

A. See text.

Page 6

Q. Describe the white cells.

A. See text.

Q. Describe the third corpuscles.

A. See text.

Page 10

Q. Define laking of the blood and mention some of the laking agents.

A. See text.

Q. What is hemoglobin and its important physiological property?

A. The real coloring substance of the red cells. Its power to form an easily disassociable compound with oxygen.

Q. In what two forms may oxygen be combined with hemoglobin?

A. As the easily disassociable form of oxyhemoglobin and the more stable form of methemoglobin.

Page 12

Q. What is carbon monoxid hemoglobin?

A. A combination of carbon monoxid and hemoglobin. The combination is a very stable one, depriving the hemoglobin of its power to unite with oxygen.

Page 14

Q. How may these various forms of hemoglobin be recognized?

A. By their characteristic spectra.

Page 18

Q. What tissues form the red blood cells?

A. In the embryo the mesenchymic cells, which form the earliest vessels; later in the fetus, in the liver, spleen and bone marrow, and finally after birth the bone marrow.

Page 22

Q. What are the varieties of the white cells?

A. See text.

Page 24

Q. Where are the white cells formed?

A. The lymphocytes in the lymph glands, the neutrophiles and eosinophiles in the bone marrow.

Page 30

Q. What are the blood plaques?

A. Small globular structures about one-third the size of a blood cell,

with apparent organization containing a central more highly refractile and darker staining portion and a surrounding protoplasmic-like body, presenting star-like angles at its periphery, from which fibers may radiate. It is probable that they do not exist in the circulating blood, but are proteins of the blood precipitated by shedding which contribute toward the clotting process.

Page 34

Q. What methods or agents will prevent blood from clotting?

A. See text.

Q. What is the mechanism of clotting?

A. The formation of a mesh-work of fibrin by a combination of thrombin with fibrinogen, the thrombin itself being first formed from prothrombin in the presence of lime salts. In the circulating blood prothrombin does not form thrombin, because of the presence of sufficient antithrombin. In shed blood a substance called by Howell a thromboplastic substance, and by others thrombokinase, is formed which either (Howell view) neutralizes antithrombin, or (other views) forms in the presence of lime salts thrombin by reacting with prothrombin or thrombogen.

Page 44

Q. How do the various anti-coagulants act?

A. See text.

Page 48

Q. What is the reaction of blood?

A. Very slightly alkaline to litmus, or as estimated by the electrical method.

Page 50

Q. Give the composition of blood.

A. Fibrin $\left\{\begin{array}{l}\text{Fibrinogen}\\ \text{Thrombin}\end{array}\right.$

Serum $\left\{\begin{array}{l}\text{Serum albumen}\\ \text{Serum globulins}\end{array}\right.$

Red and white cells
Total proteins about 8 parts.
Salts, 1 part; of these Sodium chlorid 60%
Sodium carbonate 30%
Potassium, Calcium, traces
Phosphates 0.512

Page 54

Q. What are the four kinds of vessels transporting the blood, and how do they differ, and what is their function?

A. Arteries, large vessels with thick muscular and relatively large amounts of elastic tissue, the largest of these vessels having relatively less muscle and capable of changing their diameter but little. The arterioles, very small vessels, the media of which is pure muscle. They are capable of large changes in their diameter. The capillaries, about the same diameter as the arterioles, but far more numerous, so that their total sectional area is greater. They possess very thin walls, containing no muscle, their walls being merely a single layer of endothelial cells. The veins, varying in size from minute venules to

large vessels, but all possessing very thin walls, and incapable of much distention and of no active changes in the size of their lumen. The arteries convey the blood from the heart to the capillaries, and veins carry the blood from the capillaries back to the heart. The capillaries permit of diffusion to and from the extra capillary by single space.

Q. In the mammal what arrangement of the circulation exists for the assimilation of oxygen?

A. A separate portion of the circulation conveying the blood by the pulmonary artery from a special ventricle, for this purpose the right ventricle, to the lungs, and a special set of veins, the pulmonary veins, by which it is returned to the left side of the heart. In the lungs the blood is spread out in a capillary network in very thin partitions between adjacent air spaces.

Page 60

Q. How do the veins and arteries react to intravascular pressure?

A. 80 mm. of Hg will cause a 50% distention of the arteries, and only 130 to 160 mm. will completely distend them, while 1 or 2 mm. of Hg will cause a 50% distention of the veins, and 50 mm. will completely distend them. However, a few additional mm. of Hg to 1 or 2 will so distend the veins that they will contain very little more blood on complete distention.

Q. How are blood pressures measured? What is meant by systolic, diastolic and pulse pressure, and how much are these in the human body?

A. Directly by connecting the open end of the artery to a mercury manometer, a citrate solution intervening between the blood and the mercury.

Indirectly by determining when the arterial pulsation disappears distal to a point of compression by pneumatic pressure in series with a manometer.

Systolic pressure is the highest pressure reached in the artery. It is produced by the ventricular contraction of the heart.

Diastolic blood pressure is pressure within the artery coincident with the closure of the aortic valves. The sudden fling back of the aortic valves as their closure is permitted by the fall of the pressure within the left ventricle, the fall being accompanied with a release of the intravascular pressure on the walls of the artery. There occurs at this time a sudden drop in blood pressure, followed by a slight rise, and the blood recoils from the valve as the arterial wall contracts upon it. This sudden drop marks the diastolic pressure. It may be measured by noting the height of the mercury in the manometer at the time of the transmission of a sound wave to a stethoscope placed on the wall of the artery below the constricting air cushion of the manometer, or by the level of the mercury at the time of the sudden falling off of the pulsations in the manometer. The pulse pressure is the difference between the systolic and diastolic pressures.

The systolic pressure is about 120 mm.
The diastolic pressure is 75 to 85 mm.
Thus leaving a pulse pressure of 40 mm.

Page 62

Q. Where does the blood meet with the greatest fall of pressure in its passage through the vascular system, and what is the function served by this provision?

A. In the arterioles. These vessels control the blood pressure.

THE CIRCULATION

Page 70

Q. What are the actual pressures in the various portions of the vascular system?

A. See text.

Page 72

Q. Upon what does the proper nutrition of the tissues depend?

A. Upon rapidity and volume of the capillary circulation.

Q. What are the factors controlling the rapidity and volume of the capillary circulation?

A. Primary factors:
1. The force of heart beat.
2. The caliber of the arterioles.

Secondary factors:
1. Volume of venous return to the heart.
2. The quantity of blood sequestrated in the capillaries.
3. Hydrostatic pressure in the veins.
4. The heart rate and relation of the diastolic period to the cardiac cycle.

Page 74

Q. Explain the sequence of events following excessive contraction of the arteries.

A. 1. A very high blood pressure in the arteries.

2. A response on the part of the heart by a stronger beat, so that for a time the same amount of blood is forced through the arterioles to the capillaries.

3. When the compensation on the part of the heart becomes insufficient, the quota of blood failing to make up the normal quantity which should leave the heart becomes dammed back into the venous system.

There then occurs a higher pressure in the capillaries and they become dilated and as a result the speed and volume of the capillary circulation is reduced.

Page 76

Q. Explain the sequence of events following excessive dilatation of the arterioles.

A. 1. A sudden slight reduction of arterial blood pressure, due to the increased space within the arterial portion of the circulation.

2. A still further decrease of arterial pressure, due to a sudden distention of the capillaries, caused by the sudden inrush of blood at a higher pressure into them from the dilated arterioles.

3. If the condition is unrelieved by a return of the normal degree of contraction of the arterioles there occurs a loss of tone in the capillary system, in virtue of which they become incapable of again contracting, and permanent diminution of the speed and volume of the capillary circulation ensues.

Page 86

Q. Describe the anatomy of the heart and the course of the blood through it.

A. See text.

THE CIRCULATION

Page 102

Q. Describe the cardiac cycle and the relative duration of the various events of the cycle.

A. See text.

Page 114

Q. Describe the position of the heart in the chest, and its shape in contracted and relaxed condition.

A. See text.

Page 116

Q. What causes the apex beat?

A. See text.

Q. What is a cardiometer?

A. An instrument for making a graphic representation of the changes in the cardiac muscle during contraction.

Q. Describe the three heart sounds and the time of their occurrence in the cardiac cycle.

A. See text.

Page 120

Q. What are the factors responsible for the return of the blood to the heart?

A. The pressure in the great veins, depending in turn upon (see text).

Page 126

Q. What is the pulse wave, and its cause?

A. The transmission of a circular wave of dilatation from one end of the artery to the other. It is due to the molecular transmission of the force of the impact of the systolic discharge.

Page 128

Q. What is the difference between the pulse wave and the flow of the blood through the artery?

A. One is the transmission of distending force from molecule to molecule, and the other the transmission of the molecules themselves.

Page 130

Q. How is the pulse wave recorded? And draw a typical pulse curve.

A. See text.

Page 134

Q. What are the factors which change the character of the pulse curve, and the character of the changes produced by them?

A. 1. The degree of peripheral resistance offered to the ventricle.
2. The strength and rapidity of the ventricular contraction.
3. The volume of blood discharged by each ventricular contraction.
4. The efficiency of the valves.

A high peripheral resistance diminishes the steepness of the systolic and diastolic curves. The steepness of the curves is also proportional to the strength of the heart beat, and inversely proportional to the quantity of blood discharged at each systole. The position and depth of the secondary de-

pression in the pulse curve depend chiefly upon the peripheral resistance. The chief secondary wave is called the dicrotic wave, and corresponds to the closure of the aortic valves. There are also pre- and postdicrotic waves, due to oscillations as the intraventricular pressure suddenly rises and falls they become less marked proportionally to the distance from the heart that the record is made. They are proportional in amplitude to peripheral resistance, the volume of blood discharged and strength of ventricular contraction, and inversely proportional to the competency of the valves. In time of appearance on the primary wave they are proportional to the degree of peripheral resistance. When occurring on the ascending wave or near to it, the pulse is anacrotic, and when later on descending wave, catacrotic.

Page 138

Q. What are the different varieties of pulse?

A. See text.

Page 142

Q. What is the effect of saline infusion, and how does infusion differ from transfusion?

A. A temporary increase in arterial and venous pressure disproportional to amount of fluid injected. Transfusion a more permanent increase of arterial and venous pressure.

Page 146

Q. What are the special characters of the pulmonary circulation?

A. See text.

Q. What is the effect of the phases of respiration on the arterial blood pressure?

A. Inspiration increases the influx of blood to the right auricle and to the lungs. This excess is discharged immediately into the left side of the heart and through it into the arterial circulation, and thus increasing the arterial blood pressure during inspiration, an increase beginning and ending slightly after the beginning and ending of inspiration.

Page 148

Q. How may the flow of blood through the arterioles, capillaries and veins be distinguished?

A. See text.

Page 152

Q. How are increments in hydrostatic pressure compensated for in connection with the return of blood from the capillaries?

A. By a combination of the effect of the valves in the veins and the equalizing effect of equal differences in pressure in the veins and arteries, a force being contributed to by the external support furnished to the walls of the veins by the fascial planes and muscle contraction, and finally by the contraction of the arterioles, the latter being probably the most important factor.

Page 156

Q. What is the character of the venous pulse?

A. Three waves, a large one due to auricular contraction, another equally high, due to ventricular contraction, and a small one, due to filling of auricle.

THE CIRCULATION

Page 158

Q. What is the great functional characteristic of heart muscle, and how is this character exhibited by the various portions of the heart muscle?

A. Its power of originating its own contraction, a property exhibited in descending scale from the sinus venosus to the apex of the ventricle.

Q. What nervous tissue exists in the heart and what influence does it have upon the heart action?

A. The ganglion of Remak in the sinus venosus and the ganglion of Bidder in the auriculoventricular groove. The nerve fibers of the vagus system ending around the cells of these ganglia and the postganglionic axons carrying onward the impulses of the vagus system, also the nerves of the sympathetic nervous system ending in the heart. The nerves of the heart have nothing to do with originating the cardiac contraction, nor with transmitting the stimulus to contraction over the whole heart. Their impulses merely modify its rate and force, the vagus showing the heart rate, the sympathetic accelerating the rate and generally strengthening the force of the beat.

Page 164

Q. What is the course taken by the wave of contraction through the heart?

A. The impulse to contraction starts in the sinus venosus and follows in the sequence of the normal order of the embryological units through the whole heart, passing from the sinus to the auricles, then to the ventricles, and then to the bulbus arteriosus.

Page 166

Q. How is the exact path of the wave of excitation mapped out, and what is this path, and the character of the tissue transmitting the impulse to contraction?

A. By the electrocardiogram which detects exact time relations in the passage of a diphasic current accompanying the wave of excitation as it passes over any two spots in the heart muscle upon which the electrodes of the electrocardiogram are placed. The exact path of the wave of excitation begins in the sino-auricular node, and spreads along the fibers radiating from this point, at equal rates in various directions, until the impulse reaches the auriculo-ventricular node, which is situated below and to the right of the coronary sinus. From here it spreads by a special bundle of more primitive and easily distinguishable fibers of heart muscle, known as the bundle of His, along the top of the auriculo-ventricular septum to all parts of the ventricle, the last portion of the heart to receive the impulse through them being the bulbus arteriosus.

Page 204

Q. What effect do varying percentages of carbon dioxid have on the heart?

A. See text.

Page 208

Q. What is the effect on the heart action of stimulation of the peripheral end of the divided vagus?

A. The heart is slowed and each beat is more forcible. It may be

stopped altogether. If the stimulation is not too strong the heart may begin to escape from the influence of the vagus.

Page 216

Q. What is the action of the sympathetic nerves on the heart?

A. The impulses of the sympathetic nerves quicken the heart and slightly increase its force.

Page 220

Q. What effects follow stimulation of the central end of these depressor fibers, i. e., the central end of the vagus?

A. See text.

Page 224

Q. What is the most important afferent path of depressor impulses, and to what center do they pass?

A. In the vagus nerve the depressor fibers, beginning on the wall of the heart and aorta, to the cardio-inhibitory center in the medulla and vasomotor center.

Q. What is the efferent path from the cardio-inhibitory and vasomotor centers?

A. The vagus nerve itself and vasomotor nerves.

Page 228

Q. What is the effect of muscular exercise on the heart action, and the explanation of this effect?

A. See text.

Q. What is the explanation of second wind?

A. See text.

Page 232

Q. Give a brief description of the anatomy of the sympathetic nervous system.

A. See text.

Page 234

Q. State a simple experiment which demonstrates the functions of the sympathetic nervous system.

A. See text.

Page 236

Q. Where is the vasomotor center, and how may its existence at this place be demonstrated?

A. See text.

Q. What does the term center in connection with the vasomotor function mean?

A. A region in the medulla not necessarily limited to any isolated place in it from which all efferent vasoconstriction impulses have their starting place. Its existence makes for the more efficient performance of vasomotor functions, as it represents a central depot where all afferent impulses related to vascular changes may be received, and provoke a unified efferent response to all portions of the body.

Page 238

Q. What effect does a lack of oxygen or increase of carbon dioxid produce on the vasomotor center?

A. Both stimulate the center and, therefore, increase vasomotor constriction.

Page 242

Q. What effect does an increase of lactic acid produce on the vasomotor center?

A. It stimulates it and, therefore, produces vasomotor constriction.

Page 246

Q. To what extent are vasomotor functions performed by the cord?

A. See text.

Page 250

Q. What vasoconstrictor functions may take place for which the vessel wall itself is responsible?

A. There is a purely myogenetic response to differences in intravascular pressures.

Page 252

Q. In addition to the vasoconstrictor mechanism does the neurovascular apparatus possess a vasodilatation mechanism? Illustrate.

A. Yes, and chorda tympani and the nervi erigentes.

Page 258

Q. How may vasodilatation be estimated?

A. By fall in blood pressure and measuring the volume of an organ by its displacing capacity in a plethysmograph.

Page 262

Q. How may vasodilator nerves to the extremities be demonstrated?

A. See text.

Q. What relation do the vasodilator nerves bear to the post spinal roots?

A. Their fibers pass through the portion of the root distal to the ganglia, but not proximal to it.

Page 266

Q. What is the most important afferent tract for vasodilator functions? Describe the function served by this nerve and the method of its operation.

A. The depressor nerve, having its origin in the wall of the aorta and passing with the vagus nerve which it joins at various levels in different animals to the vasomotor center, responds chiefly to increase of pressure in the aorta and opposes an increase of arterial pressure by stimulating strong vasomotor dilatation in especially the splanchnic area. It is therefore conservative in its function, protecting the body against undue arterial pressure.

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